

Selenium influences thyroid hormones, myricetin has anti-cancer effects on human papillary thyroid cancer cells, and thyroid hormones have been associated with psychological disorders: Thyroid evaluation and therapy during pregnancy

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World Journal of Advanced Research and Reviews, 2023, 19(03), 1298–1308

Publication history: Received on 18 August 2023; revised on 26 September 2023; accepted on 28 September 2023

Article DOI: <https://doi.org/10.30574/wjarr.2023.19.3.1978>

Abstract

Introduction: A micronutrient called selenium; a non-metallic element is necessary to manufacture selenoproteins, including selenocysteine. The thyroid has the highest concentration of selenium per gram of tissue in people. The majority of known selenoproteins, including glutathione peroxidase, are expressed in the thyroid and are crucial for the metabolism of thyroid hormones, control of redox states, and preservation of cellular homeostasis. It has been demonstrated that selenium therapy for Graves orbitopathy patients can slow the disease's course and enhance the quality of life. Different selenium supplements have demonstrated varying anticancer efficacy in thyroid cancer. It also looked at how different treatment plans affected patients' thyroid function, mood, and inflammatory markers. TSH (thyroid-stimulating hormone) is slightly elevated in subclinical hypothyroidism, while T4 or T3 levels are normal.

Objective: The purpose of this study was to evaluate the therapeutic effects of levothyroxine sodium given alone or in combination with selenium on patients with chronic lymphocytic thyroiditis and hypothyroidism to serve as a guide for clinical treatment. The purpose of the current study is to ascertain the impact of selenium supplementation on thyroid hormone and anti-thyroid peroxidase antibody (anti-TPO AB) levels. The pathophysiology of this illness may be affected by the imbalance in the activity of T cells such as Th1, Th2, Th17, and Treg. This study was to evaluate any changes in the release of cytokines by these cells after selenium administration in patients with HT. The diagnosis and management of thyroid problems during pregnancy are covered in detail in this article. It also includes a summary of the main recommendations made by several medical associations for the diagnosis, treatment, and interpretation of thyroid function during pregnancy.

Results: The combined group's overall effective rate was much greater than the control group's. After therapy, both groups' TT3, TT4, TSH, TgAb, and TPOAb levels, SAS and SDS scores, and levels of inflammatory mediators such as IL-2, IL-10, and TNF- all showed a significant improvement. In the combination group, IL-10 levels increased more, and TgAb, TPOAb, IL-2, TNF-, SAS, and SDS scores reduced more when compared to the control group, whereas the differences in the other indices were not statistically significant. According to research, LT4 has some efficacy in treating CLT with hypothyroidism, and selenium therapy in combination with LT4 can increase its therapeutic effect and help patients' immunological and inflammatory responses as well as their mood.

Conclusions: Myo-inositol, vitamin D, and selenium supplementation together had an impact on the decline in cytokine markers, Ab-TPO, and Ab-TG levels, which helped to compensate for the underlying condition. Since myricetin is a strong inducer of HATC cell death, it may be helpful in the creation of HATC therapeutic medicines. Myricetin significantly reduced the growth of HATC cells, by almost 70%. A significant number of dead cells showed sub-G1 phase arrest. In SNU-80 HATC cells, myricetin similarly displayed cytotoxicity and caused DNA condensation in a dose-

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dependent manner. Additionally, myricetin induced the mitochondria to release apoptosis-inducing factor (AIF) into the cytoplasm and changed the potential of the mitochondrial membrane.

Keywords: Selenoproteins; Myricetin; Interpretation & management of maternal thyroid; Dysfunction of thyroid hormones associated with psychological disorder

1. Introduction

The comprehension of selenium's crucial involvement in thyroid hormone synthesis, metabolism, and action as well as in preserving healthy thyroid function has significantly improved over the past few decades. The thyroid is one of the organs with the highest selenium content due to the expression of several Selenium enzymes that are essential for preserving thyroid hormone metabolism, such as the deiodinases (DIOs), and for protecting thyroid cells from oxidative damage, such as cytosolic and plasma glutathione peroxidases (cGPx and pGPx) and phospholipid-hydroperoxide glutathione peroxidase (PHGPx).^[1]

1.1. Dietary Sources of Selenium Compounds and Their Metabolism

The most prevalent dietary Se molecules are selenomethionine (SeMet), selenocysteine (SeCys), se-methyl selenocysteine (MeSeCys), and selenite. Se in the diet can be provided in organic or inorganic forms. Vegetables, cereals, legumes, nuts, and yeast are among the foods that are high in organic forms of Se, making SeMet the predominant form in food products. Some of these foods and water have been shown to contain inorganic se, and SeMet can be found in a wide variety of foods, including wheat, meat, eggs, dairy products, nuts (particularly Brazil nuts), walnuts, and yeast.^[2]

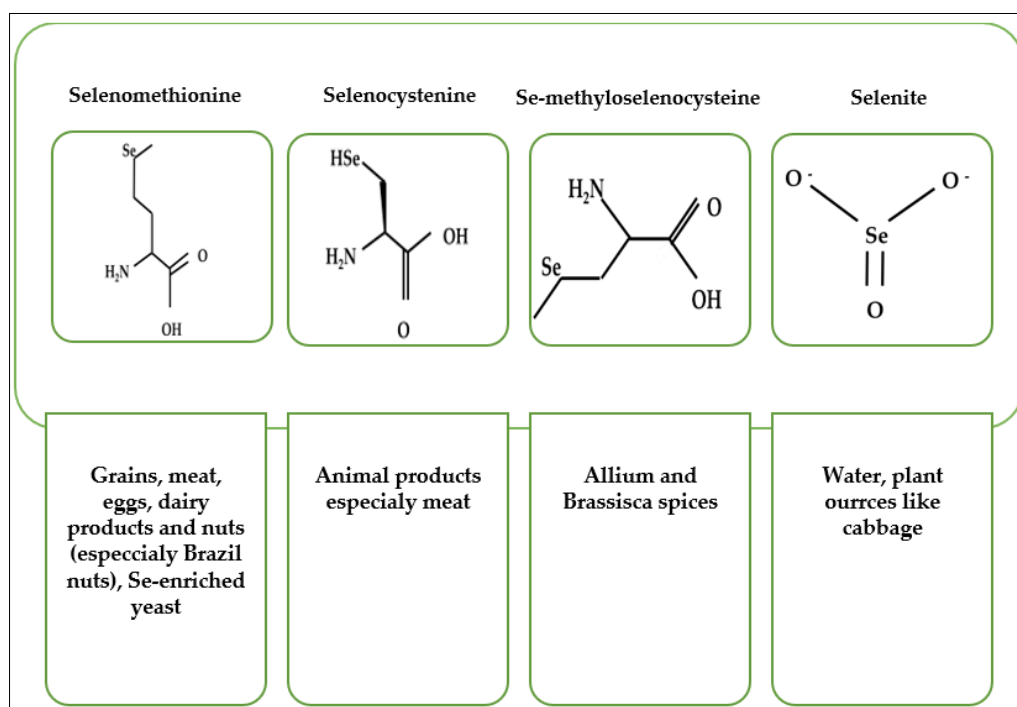


Figure 1 Dietary sources of selenium compounds.^[3]

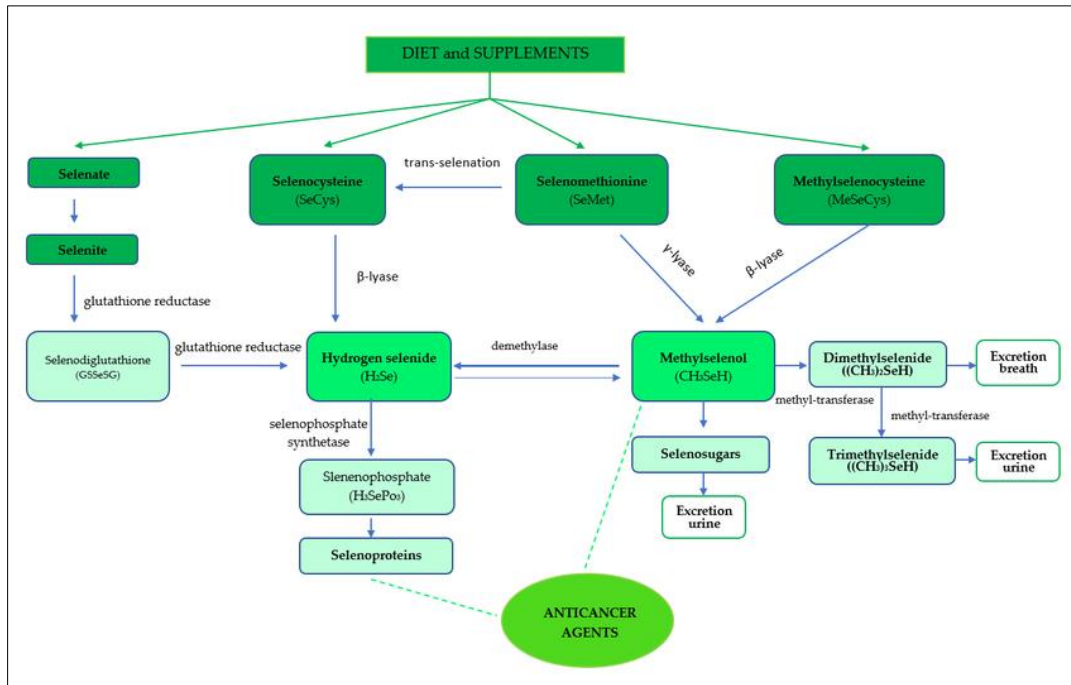


Figure 2 The metabolic pathways of selenium compounds in the human body.^[4]

Thyroid dysfunction is not linked to the classic disorders associated with extreme selenium deficiency, destructive osteoarthritis (Kashin-Beck disease), and fatal myocarditis (Keshan disease). In cases of severe selenium insufficiency, thyroid glutathione peroxidases' (GPx) activity is significantly reduced. This causes oxidative cell damage, necrosis, and the invasion of macrophages and T lymphocytes into the thyroid tissue. The thyroid is destroyed by chronic inflammation through TGF-dependent mechanisms, which causes the gland to atrophy. It is believed that even a mild-to-moderate dietary selenium deficit might cause autoimmune thyroid disorders to develop or worsen in people with a family history of developing autoimmune diseases. Selenium deficiency is accompanied by a loss of immune competence. Both cell-mediated immunity and B-cell function can be impaired.^[5]

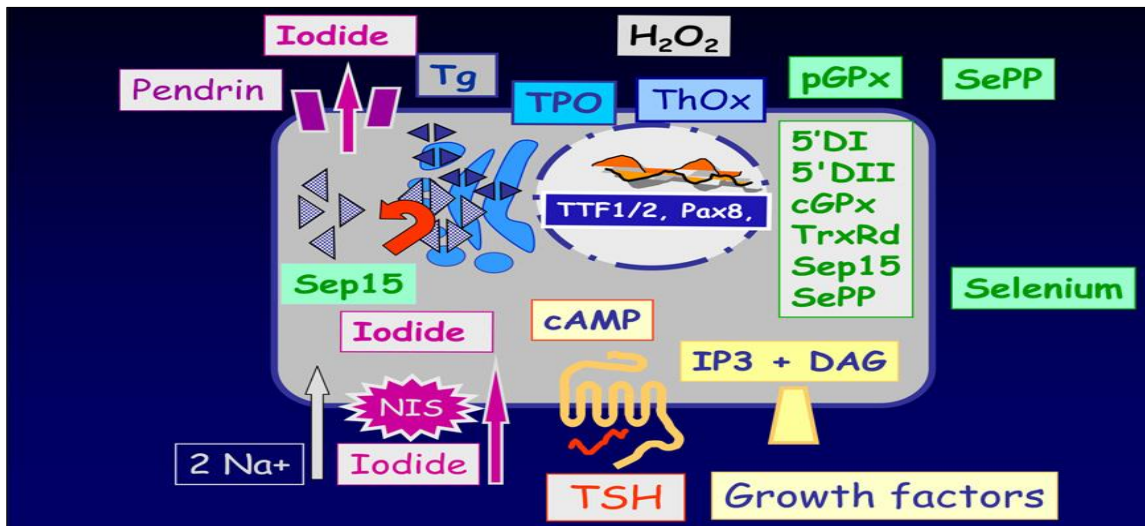


Figure 3 Relevant Proteins and Factors Involved in Thyroid Hormones Biosynthesis in Thyrocytes. Abbreviations: DAG, diacylglycerol; 50DI, type I 50-deiodinase; 50DII, type II 50-deiodinase; cGPx, cytosolic glutathione peroxidase, GPx1; pGPx, plasma glutathione peroxidase, GPx3; IP3, inositol trisphosphate; Sep15, selenoproteins 15; Sepp, selenoproteins P; Tg, thyroglobulin; ThOx, thyrooxidase, dual oxidase (DuOx); TSH, thyroid stimulating hormone, thyrotropin.^[6]

In a double-blind randomized experiment of patients with rheumatoid arthritis, supplementation with 200 mg selenomethionine daily for three months dramatically decreased pain and joint involvement, suggesting that selenium compounds may have an anti-inflammatory impact.

1.1.1. Selenium Metabolic System

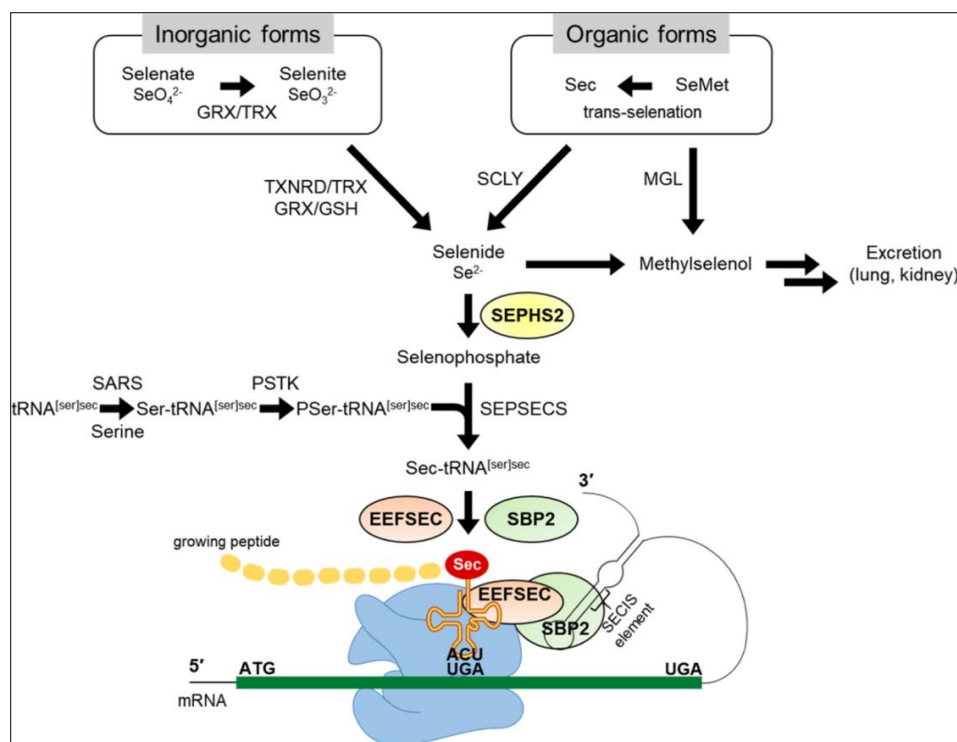


Figure 4 Selenium metabolic system

Selenium is absorbed from the diet, undergoes several conversion steps, and is incorporated into polypeptide chains, completing selenoproteins synthesis. Dietary sources of selenium uptake exist in inorganic forms such as selenate and selenite and organic forms such as Sec and SeMet. Inorganic forms are reduced by TXNRD/TRX or GRX/GSH systems & organic forms are cleaved by SCLY, forming selenide. Selenophosphate is synthesized from selenide by SEPHS2, and the subsequent reaction with P-Ser-tRNA^{[Ser]Sec} mediated by SEPSECS yields Sec-tRNA^{[Ser]Sec}. Sec-tRNA^{[Ser]Sec} is transferred to the A-site of ribosome mediated by SBP2, which binds to SECIS located in the 3'UTR of a selenoproteins mRNA. Finally, the UGA codon is recognized as the Sec integration codon. Abbreviations: SeMet, selenomethionine; Sec, selenocysteine; GRX, glutathione reductase; TRX, thioredoxin; TXNRD, thioredoxin reductase; GSH, glutathione; MGL, methionine gamma-lyase; SCLY, selenocysteine lyase; SEPHS2, Selenophosphate synthetase 2; SARS, seryl-tRNA synthetase; PSTK, phosphoryl (Sep)-tRNA kinase; SEPSECS, Sep-tRNA: Sec-tRNA synthase; EEFSEC, Sec-specific eukaryotic elongation factor; SBP2, SECIS binding protein 2.^[7]

Selenium deficiency has been linked to its etiology along with several genetic and environmental variables. For the synthesis, activation, and metabolism of thyroid hormones, selenium is a crucial vitamin. The thyroid gland accumulates more selenium per gram of tissue than any other organ. In contrast, selenium's key contribution to antioxidant defense is found in the structure of selenoproteins. Thyroid risk for illness is raised with selenium deficiency, particularly in the conversion of T4 into T3. In patients with Hashimoto's disease and pregnant women with elevated anti-thyroid peroxidase antibodies (anti-TPO Ab), selenium supplementation reduces anti-thyroid antibody levels. Selenium supplementation has been shown to reduce the incidence of postpartum and hypothyroid thyroiditis in pregnant women.^[8]

Studies indicate that patients receiving typical treatments have plasma selenium levels that are significantly lower than those of the general population, and that selenium has proved clinically effective in treating thyroid problems. Furthermore, it has been demonstrated that moderate dietary selenium intake can lift the mood of the general populace and that inadequate selenium intake has been associated with an increased risk of major depression and depressed mood in women.

The most prevalent endocrine malignancy, thyroid cancer, has gradually increased in incidence during the past three decades. An estimated 1 to 2 instances of anaplastic thyroid carcinoma (ATC) are diagnosed annually in one million people. An abundant flavonoid found in fruits and vegetables called myricetin has been shown to have anti-cancer properties. According to earlier research, myricetin causes apoptosis in several cancer cell types, including colon, hepatoma, pancreatic, and oesophageal cancer. Myricetin causes the death of human colon cancer cells through Bax- and Bcl-2-dependent pathways, as we previously observed. Human anaplastic thyroid cancer (HATC) cell line SNU-80 was used to test myricetin's anticancer properties. Investigations were also made on the mechanism behind myricetin's anticancer properties. The results of this study indicate that myricetin may be an effective chemotherapeutic drug in the treatment of human ATC.^[9]

1.2. Interpretation of the thyroid during pregnancy

Gynecologists and general physicians frequently encounter thyroid issues during pregnancy in the course of their daily work.

1.2.1. Pregnancy thyroid disorder consists of

- Hypothyroidism
- Subclinical hypothyroidism
- Hyperthyroidism
- Hyperemesis gravidarum
- Thyroid nodule
- Postpartum thyroiditis

In pregnancy, subclinical hypothyroidism is the most prevalent thyroid condition. The need for thyroxine is larger in pregnant women than in non-pregnant women because of the complicated hormonal changes that occur during pregnancy. Pregnancy safety with minimal maternal and neonatal complications is ensured by the treatment of thyroid disorders.

Table 1 Changes in Thyroid Function test results during uncomplicated pregnancy & and in pregnant women with thyroid disease.^[10]

Maternal condition	Thyroid stimulating Hormone	Free Thyroxine	Free Thyroxine index	Total thyroxine	Triiodothyronine	Resin triiodothyronine uptake
Hyperthyroidism	Decrease	Increase	Increase	Increase	Increase or no changes	Increase
Hypothyroidism	Increase	Decrease	Decrease	Decrease	Decrease or no change	Decrease
Normal pregnancy	Decrease	No change	No Change	Increase	Increase	Decrease

1.2.2. Screening for thyroid disorder during pregnancy

- As advised by various societies, all pregnant women should be checked at their first antenatal appointment by monitoring their TSH levels.
- In high-risk populations, such as females with a personal history of thyroid or other autoimmune disorders, women with goiter, women with a history of miscarriage or premature delivery, or females with type 1 DM, the anti-TPO antibodies should be taken into consideration.
- There is not much evidence for giving corticosteroids or LT4 therapy to patients with positive anti-TPO antibodies and normal TSH.

Table 2 Trimester-specific ranges for TSH levels.^[11]

Trimester	TSH Range
First trimester	>0.1 mIU/L and <2.5 mIU/L
Second trimester	>0.2 mIU/L and <3.0 mIU/L
Third trimester	>0.3 mIU/L and <3.0 mIU/L

1.2.3. Management of hypothyroidism during Pregnancy: - ^[12]

- The fetus is known to experience substantial negative effects from overt hypothyroidism. As a result, recommendations should be followed when treating hypothyroidism.
- Levothyroxine (LT4) should be utilized to manage subclinical hypothyroidism, defined as serum TSH over the upper limit of the trimester-specific reference range with normal T4. This is because SCH may have negative effects on both the mother and the fetus.
- The dosage of LT4 frequently needs to be increased by 4 to 6 weeks of gestation and may need to be increased by 30% or more.
- If overt hypothyroidism is diagnosed during pregnancy, The LT4 dose (1.6-2.0 g/kg/d) should be appropriately titrated to achieve the appropriate trimester-specific TSH ranges. TFT needs to be assessed within 30–40 days, and then every 4–6 weeks after that.
- Most hypothyroid women need to reduce their LT4 dosage to pre-pregnancy levels after giving birth.
- Every trimester, TSH levels should be monitored for women with thyroid immunity who are euthyroid in the early stages of pregnancy since they have a higher chance of developing hypothyroidism.

1.2.4. Maternal Hyperthyroidism: Maternal aspect

- Due to the negative effects of overt hyperthyroidism on the mother and fetus, hyperthyroidism must be distinguished from both normal pregnancy physiology and gestational thyrotoxicosis if a subnormal serum TSH value is found during gestation.
- Clinical evidence of autoimmunity, a typical goiter, and the presence of TSH receptor antibodies (TRAb) all help to distinguish Graves' disease from pregnant thyrotoxicosis. In either scenario, TPO-Ab might be present.
- Subclinical hyperthyroidism during pregnancy does not require treatment because there is no evidence that treating so will lead to a healthier pregnancy.
- Propylthiouracil (PTU) in the first trimester and methimazole (MMI) from the second trimester onwards should be used to treat overt hyperthyroidism. Patients who cannot tolerate PTU or who have an unfavorable reaction to PTU may choose to explore MMI. 100–150 mg of PTU is equivalent to 10 mg of MMI.
- Beta-blockers should only be used to treat the symptoms of thyrotoxicosis or wait for the effects of surgery or anti-thyroid medication because they have long-term adverse effects. Propranolol (40–120 mg per day in divided doses) is the most frequently utilized beta-blocker.
- Reassessing the TRAb level at the beginning of pregnancy is advised in cases where hyperthyroidism was previously treated with ablative therapy to rule out the possibility of fetal or post-natal hyper- or hypothyroidism.
- Indications for subtotal thyroidectomy as a Graves's Disease treatment during pregnancy (often during the second trimester) include the following:
 - The patient's adverse reaction to ATD therapy is significant.
 - ATD must be administered continuously at large doses (more than 30 mg/d of MMI or 450 mg/d of PTU).
 - The patient's uncontrolled hyperthyroidism and non-adherence to ATD medication.

1.2.5. Maternal Hyperthyroidism: Fetal aspect

- Foetal thyrotoxicosis is brought on by thyroid receptor antibodies, which can easily cross the placenta and stimulate the fetal thyroid. The mother's levels of these antibodies need to be evaluated using
 - Current Graves' disease
 - A history of Graves' disease and

- treatment with 131I or
 - thyroidectomy before pregnancy
 - A previous neonate with Graves' disease
 - A previously elevated TRAb
- There is extremely little chance of fetal or neonatal thyroid dysfunction in women who have negative TRAb results and do not need ATD.
 - Iodide shouldn't be administered to pregnant women because it can cause fetal goiter.
 - Using iodine 131 is not suggested since radiation can have teratogenic consequences during pregnancy.
 - Foetal thyrotoxicosis should be evaluated by FHR (> 160 bpm) in cases where the mother is euthyroid but positive for TRAb. Start the mother on methimazole/carbimazole to treat fetal thyrotoxicosis and LT4 to maintain maternal euthyroidism if all other potential causes of fetal tachycardia have been ruled out.
 - The treating physician needs to begin ATD therapy for the mother as soon as fetal hyperthyroidism is identified. In two weeks, the fetus should have another USG evaluation to see whether there has been a clinically significant improvement.

1.2.6. *Thyroid nodules in pregnancy* ^[13]

- The evaluation of a palpable thyroid nodule should include tests of serum TSH, a thyroid gland USG, and, if required, FNAC.
- If the nodule is benign, no further testing is necessary; however, if the TSH is elevated, LT4 should be provided to return the TSH to normal.
- In the second trimester, surgery should be considered if the nodule turns out to be malignant or exhibits rapid growth.
- Following surgery, patients should continue receiving LT4 therapy while monitoring their TSH and free T4 levels every six weeks.
- Radioiodine remnant ablation and postoperative whole-body Iodine-131 scintigraphy are not advised during pregnancy or lactation.

1.2.7. *Postpartum thyroiditis*

Within a year of birth, postpartum thyroiditis is characterized by thyroid dysfunction, which may include clinical signs of hyperthyroidism, hypothyroidism, or combined hyperthyroidism and hypothyroidism.

- Due to a paucity of information, screening for postpartum thyroiditis is not advised for all women. Since PPT is more prevalent among women with type 1 diabetes, Grave's disease in remission, and chronic viral hepatitis than in the general population, TSH screening is indicated at 3- and 6 months following birth.
- Within 12 to 18 months of the commencement of symptoms, thyroid function recovers to normal in the majority of postpartum thyroiditis cases.
- Most women in the hyperthyroid phase who experience symptoms like weariness, irritability, weight loss, palpitations, or heat intolerance don't need active ATD management; instead, these symptomatic individuals should be treated with a brief course of beta blockers, particularly propranolol.
- The hyperthyroid symptoms of fatigue, irritation, weight loss, palpitations, or heat intolerance may result from postpartum thyroiditis.
 - Typically, the thyrotoxic phase lasts only a few months and affected women frequently only have moderate symptoms.
 - The mother should receive therapy from LT4 for about a year after giving birth or until she has had all of her children. There isn't any conclusive evidence connecting thyroid antibodies or PPT to postpartum depression.
 - Women who have experienced postpartum depression should be screened for hypothyroidism and treated accordingly.

1.2.8. *Gestational Hyperemesis & Hyperthyroidism* ^[14]

- Due to the TSH receptor being stimulated by the high quantity of beta HCG, many women with hyperemesis gravidarum have abnormally low TSH levels and high serum T4 levels.

- All patients with hyperemesis gravidarum should undergo TFT since they run the risk of developing temporary hyperthyroidism.
- Most people just need symptomatic treatment for this illness, which is typically self-limiting and does not call for anti-thyroid medication. Based on the absence of classic hyperthyroidism symptoms and signs, the lack of goiter, and thyroid antibodies, it can be distinguished from intrinsic thyroid illness.

1.2.9. Autoimmune thyroid disease if pregnancy

It is not necessary to routinely screen for and treat autoimmune thyroid disease in pregnant euthyroid women.

- The Recommended Dietary Allowance (RDA) and Median Urinary Iodine (MUI) Reference Values for Adequate Iodine Nutrition in Pregnancy have been updated by the World Health Organisation from 150 to 250 g/L, respectively.
- Iodine during pregnancy is allowed in amounts of 200 to 250 g/L (RDA). When treating thyroid abnormalities in pregnancy, accurate interpretation of the thyroid profile and prompt treatment are crucial.
- To prevent the difficulties linked to thyroid issues in pregnancy, patients must be referred to an endocrinologist for management.

1.3. Thyroid Hormones

By binding to nuclear ligand receptors, thyroid hormones cause the synthesis of a nuclear ligand-activated transcription factor. Thyroid hormones are available in several quantities and forms, and they have long been used as supplemental agents to depression drugs, either to boost their effectiveness in individuals who are not responding as well to treatment or to speed the commencement of action. Thyroid hormone imbalances have long been associated with depression. Due to their ability to influence neuronal organization, arborization, and synapse development—which may have the subsequent consequence of boosting monoamine neurotransmitters—thyroid hormones may enhance antidepressant effectiveness in some people. Treatments for unipolar or bipolar depression that include thyroid hormone augmentation have fallen out of favor recently. Levothyroxine (Synthroid, Levothroid, Levoxine) and liothyronine (Cytomel) are thyroid hormones that are used in psychiatry to treat people who have depression or rapid-cycling bipolar I disorder, either alone or in combination with other medications. They can change a person's response to antidepressants from nonresponsive to responsive. For patients taking lithium, thyroid hormone replacement treatment is also utilized. Patients who receive triiodothyronine (T3) are twice as likely to respond to antidepressant therapy as those who receive a placebo. These investigations have demonstrated that the addition of T3 to the treatment regimen improves the efficacy of SSRIs and tricyclic antidepressants. However, because of issues including osteoporosis and heart arrhythmias, many endocrinologists are opposed to utilizing thyroid hormones to supplement antidepressants.

1.3.1. Pharmacologic actions

Thyroid hormones are taken orally, and different amounts of them are absorbed from the GI tract. The drug's absorption is enhanced if taken on an empty stomach. Thyroxine (T4) diffuses into neurons in the brain, transforming it to T3, the physiologically active form, after crossing the blood-brain barrier. T4 and T3 each have a half-life of 6 to 7 days and 1 to 2 days, respectively. It is uncertain how thyroid hormones affect the effectiveness of antidepressants. The intracellular receptors that the thyroid hormone binds to control the transcription of a variety of genes, including various receptors for neurotransmitters.

1.3.2. Therapeutic indications

Liothyronine is added to the patient's antidepressant treatment at 25 or 50 µg daily dosage. Liothyronine has traditionally been utilized as an adjuvant for tricyclic medications, but data suggests that it also enhances the effectiveness of all antidepressant medications.^[15]

1.3.3. Precautions and adverse reactions

Adverse effects are rare at the levels usually prescribed for augmentation 25 or 50 µg per day. Transient headache, weight loss, palpitations, nervousness, diarrhea, abdominal cramps, sweating, tachycardia, elevated blood pressure, tremors, and insomnia are the most frequent side effects connected with thyroid hormones. Long-term treatment may also cause osteoporosis, but trials using liothyronine augmentation have not discovered this. Thyroid hormone overdoses can cause heart collapse and death. Patients who have cardiovascular disease, angina, or hypertension

shouldn't consume thyroid hormones. The use of hormones is not recommended in cases of thyrotoxicosis, untreated adrenal insufficiency, and sudden myocardial infarction.

1.3.4. Use during lactation and pregnancy

Pregnant women can receive thyroid hormones without risk as long as laboratory thyroid indices are maintained and monitored properly. There is very little thyroid hormone excretion in breast milk, and it has not been established that this causes issues for newborns who are breastfed.

1.3.5. Drug interactions

By enhancing the breakdown of coagulation factors, thyroid hormones can intensify the effects of warfarin (Coumadin) and other anticoagulants. They might make it more necessary for diabetics to take insulin and for people with heart problems to take digitalis. Due to the possibility of cardiac decompensation, sympathomimetic drugs like ketamine (Ketalar) and maprotiline (Ludiomil) should not be taken alongside thyroid hormones. In people who are euthyroid or on thyroid replacement therapy, the administration of SSRIs, tricyclic and tetracyclic medications, lithium, or carbamazepine (Tegretol) can slightly drop serum T4 and increase serum thyrotropin concentrations. Due to this interaction, thyroid hormone supplementation may need to be started or increased in dosage, as well as close serum monitoring.

1.3.6. Laboratory interferences

Other than thyroid function indexes, no laboratory test has been reported to be affected by levothyroxine. However, liothyronine inhibits the production of endogenous T4, which lowers the outcome of any thyroid function test that depends upon the measurement of T4. According to certain research, up to 10% of individuals who reported feeling depressed and fatigued had early hypothyroidism. Hypothyroidism and hyperthyroidism are both conditions that lithium can lead to. Intellectual disability caused by neonatal hypothyroidism can be avoided if the diagnosis is diagnosed at birth.

1.3.7. Thyrotropin-Releasing Hormone Stimulation Test

Patients with suspected subclinical hypothyroidism and mildly abnormal thyroid test findings, which may explain clinical depression, are advised to undergo the thyrotropin-releasing hormone (TRH) stimulation test. Additionally, it is applied to patients who may have hypothyroidism brought on by lithium. 500 mg of protirelin (TRH) is injected intravenously during the procedure, and serum TSH levels are then tested at 15, 30, 60, and 90 minutes after the injection. It is typical to have a rise in serum TSH of 5 to 25 mIU/mL from baseline. A diagnosis of depression may be associated with a muted response, which is defined as a rise of less than 7 mIU/mL. Eight percent of those who suffer from depression also have thyroid disease.

1.3.8. Dosage and clinical guidelines

Liothyronine is available as tablets weighing 5, 25, and 50 µg. Levothyroxine comes in tablet forms of 12.5, 25, 50, 75, 88, 100, 112, 125, 150, 175, 200, and 300 µg. It's also available in parenteral forms of 200 and 500 µg. Liothyronine is added to the person's antidepressant treatment at a dosage of 25 or 50 g per day. All of the antidepressant medications currently on the market have been combined with liothyronine. Liothyronine supplementation trials should last two to three weeks to be effective. If liothyronine supplementation is effective, it should be continued for another two months before being gradually discontinued at a rate of 12.5 µg per day every three to seven days.^[16]

2. Materials & Methods

According to numerous research investigation articles and clinical investigations published in the literature, myricetin has anti-cancer properties on human papillary thyroid cancer cells, and thyroid hormones have been associated with psychological disorders. Thyroid assessment and therapy during pregnancy. Searches on Google Scholar, PubMed, Research Gate, and other online databases terms like the "selenium effect on thyroid hormones," "myricetin has anticancer activity," "interpretation & therapy of thyroid during pregnancy," and "dysfunction of thyroid hormones causes psychological disorder." The validity of the impacts was established by analyzing the methods of each study.

3. Results

The overall effective rate of the combined group was much higher than that of the control group. Following treatment, there was a significant improvement in both groups' TT3, TT4, TSH, TgAb, and TPOAb levels, SAS, SDS scores, and levels

of inflammatory mediators such IL-2, IL-10, and TNF-. In contrast to the control group, the combination group had higher levels of IL-10 and lower levels of TGAb, TPOAb, IL-2, TNF-, SAS, and SDS scores; however, these changes were not statistically significant. According to studies, selenium therapy combined with LT4 can boost its therapeutic effect and benefit patients' immunological and inflammatory responses as well as their mood. LT4 shows some efficacy in treating CLT with hypothyroidism. The rate of hypothyroidism recovery was significantly higher when thyroxine, iodine, and selenium were combined with or without walnut leaf powder. It is important to note that all AIT patients had their cytokine status altered, with some differences depending on the clinical presentation of the illness. After three months of treatment, a significant difference between the indicators for patients in the first group receiving Myo-inositol at a dose of 2000 mg/day, cholecalciferol at a dose of 2000 IU/day, and selenium at a dose of 100 g/day and patients in the second group receiving only cholecalciferol at a dose of 2000 IU/day and selenium at a dose of 100 g/day was found. The proliferation of HATC cells was greatly slowed down by myricetin, by about 70%. Dead cells in significant numbers displayed sub-G1 phase arrest. Myricetin similarly demonstrated cytotoxicity and led to DNA condensation in SNU-80 HATC cells in a dose-dependent manner. Myricetin also altered the potential of the mitochondrial membrane and caused the mitochondria to release apoptosis-inducing factor (AIF) into the cytoplasm

4. Conclusion

Supplementation with myo-inositol, vitamin D, and selenium affected the drop in cytokine markers, Ab-TPO, and Ab-TG levels, which served to offset the underlying problem. Myricetin may be useful in the development of HATC therapeutic drugs since it strongly induces HATC cell death. Various factors, including the stage of Hashimoto's thyroiditis development, the degree of thyroid dysfunction, and dietary selenium supplementation, affect the profile of certain cytokines generated by cells engaged in the autoimmune process. Even slight variations in thyroid hormone levels within the normal range can probably be partially responsible for changes in certain cytokines, CRP, and lipid markers. More research is necessary to understand the relevance of the observed alterations in cytokine production and the effects of selenium on the immune system during Hashimoto's thyroiditis. A conclusion that taking selenium is effective in reducing the size of the goiter and that it is also related to the type of goiter because the results showed that the size of the goiter significantly decreased after selenium intake in both groups of Hashimoto's and non-Hashimoto's goiters, although the rate of reduction in the Hashimoto's type was greater than the non-Hashimoto's type. The myricetin treatment decreased the viability of the SNU-80 HATC cells and caused apoptosis through an increase in AIF release and mitochondrial dysfunctions. Because myricetin activated caspases 3, 8, and 9, it also caused the release of AIF from mitochondria into the cytosol and the production of the apoptotic gene Bax, which lowered the viability and promoted apoptosis in SNU-790 HPTC cells. In addition, SNU-790 HPTC cells treated with myricetin showed changed MMP. These findings imply that mitochondrial dysfunction is caused by caspase-dependent myricetin induction of apoptosis. The development of therapeutic medicines for the treatment of HPTC may benefit from this characteristic.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest is to be disclosed.

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