

## *International Journal of Scientific Research and Reviews*

### **A descriptive review on hypothyroidism**

**E. Jajili<sup>1\*</sup>, M. Eswar Gupta<sup>2</sup> and K. Sravani<sup>3</sup>**

<sup>1\*</sup>Assistant Professor, Pharmaceutical Chemistry, Sir C. R. Reddy College of Pharmaceutical Sciences, Shanthi Nagar, Eluru, A.P., India,  
Email: [elurujaji.pharma@gmail.com](mailto:elurujaji.pharma@gmail.com), Mobile. No: 9573698698

<sup>2</sup>Professor, Pharmaceutics, Sir C. R. Reddy College of Pharmaceutical Sciences, Shanthi Nagar, Eluru, A.P., India, Email: [meguptas@gmail.com](mailto:meguptas@gmail.com), Mobile no: 9885523760

<sup>3</sup>Assistant Professor, Pharmaceutical Chemistry, Sir C. R. Reddy College of Pharmaceutical Sciences, Shanthi Nagar, Eluru, A.P., India,  
Email: [sravanikoralla@gmail.com](mailto:sravanikoralla@gmail.com), Mobile no 9966847776

#### **ABSTRACT:**

Hypothyroidism is a common endocrine disorder due to deficiency of thyroid hormones. It is a disease encompassing all the socio-economical and cultural groups and is more commonly seen in women and people over the age of 50. Hypothyroidism is a global disease having multisystemic involvement, varied presentations and hazardous complications. Clinical manifestations of hypothyroidism range from life-threatening to no signs or symptoms. The most common symptoms in adults are fatigue, lethargy, cold, intolerance, weight gain, constipation, change in voice, and dry skin, but clinical presentation can differ with age and sex, among other factors. The standard treatment is, thyroid hormone replacement therapy with levothyroxine. However, a substantial proportion of patients who reach biochemical treatment targets have persistent complaints. This review describes the epidemiology, causes and symptoms of hypothyroidism, summarise the diagnosis and management and also how to overcome the complications of thyroid disorders.

**KEYWORDS:** Hypothyroidism, Thyroid stimulating hormone (TSH), Hashimoto's thyroiditis, Iodine deficiency.

#### **\*Corresponding author:**

#### **E. Jajili**

Assistant Professor,

Pharmaceutical Chemistry,

Sir C. R. Reddy College of Pharmaceutical Sciences,

Shanthi Nagar, Eluru, A.P., India,

Email: [elurujaji.pharma@gmail.com](mailto:elurujaji.pharma@gmail.com), Mobile. No: 9573698698

## **INTRODUCTION:**

The thyroid gland is located in the neck below the thyroid cartilage, or Adam's apple. It is an important gland because every cell in the body depends on the hormones of the thyroid gland. Hormones from the thyroid gland affect various bodily processes, including growth and development, regulation of calcium levels, and heart and digestive functions. The thyroid makes and stores three important hormones.<sup>1,2</sup>**Thyroxine (T3):** The major hormone from the thyroid, it is essential for metabolism, as well as normal growth and development.

**Triiodothyronine (T4):** A vitally important hormone, it affects heart rate, body temperature, growth, development and metabolism. The thyroid normally produces about four times more T4 than T3, but T3 is a much more powerful hormone.

**Calcitonin:** It helps to form bones and regulates calcium levels in the body.

The thyroid makes these hormones by using iodine and tyrosine. Iodine, a trace mineral, is found in many foods but is highest in kelp, eggs, strawberries and dairy foods. It is even added to table salt. Tyrosine, an amino acid, is also found in these and many soya-based foods.

Once the thyroid converts iodine and tyrosine in to hormones, they are released in to the blood stream at the command of the pituitary gland, a peanut sized gland in the brain which creates Thyroid stimulating hormone(TSH). As a result a nonfunctional pituitary gland will eventually lead to thyroid – gland-related issues. TSH will either trigger the production of thyroxine or triiodothyronine. If TSH is not present at the right levels, too much or too little of either hormone will be made.

### **Hypothyroidism**

Hypothyroidism or under active thyroid, develops when the thyroid gland fails to produce or secrete as much thyroxine (T4) as the body needs. As T4 regulates essential functions such as heart rate, digestion, physical growth and mental development, an insufficient supply of this hormone can slow life-sustaining processes, damage organs and tissues in every part of the body, and lead to life-threatening complications. However, people with thyroid problems can experience several **symptoms** given below.<sup>3,4</sup>

#### **General:**

Dry, thick skin, dry hair, fatigue, edema (puffy hand, face and eyes), cold intolerance, weight gain, hoarseness, sluggishness, headache, constipation, shortness of breath, bradycardia, arthritis and muscle cramps.

### **Neonatal cretinism:**

Developmental impairment of skeletal system and CNS, dwarfism, broad flat nose, wide set eyes, thick lips, protruding tongue, poor muscle tone, pale skin, umbilical hernia, delayed eruption of teeth, and hoarse voice.

Each individual patient may have number of these symptoms, and they will vary with the severity of the thyroid hormone deficiency and the length of time the body has been deprived of the proper amount of hormone. Most people will have a combination of these symptoms. Occasionally, some patients with hypothyroidism have no symptoms at all, or they are just so subtle that they go unnoticed.

### **Causes of hypothyroidism:**

The most common cause of hypothyroidism is Hashimoto's thyroiditis which is an autoimmune disorder. "Thyroiditis" is an inflammation of the thyroid gland. It is characterized by infiltration of the thyroid gland with T lymphocytes and autoantibodies against specific thyroid antigens such as thyroid peroxidase, thyroglobulin and TSH. Thyroiditis may also be caused by a viral infection.<sup>5</sup>

Other causes of hypothyroidism include:

**Radiation therapy to the neck area:** Treating certain cancers, such as lymphoma, requires radiation to the neck. Radiation damages the cells in the thyroid. This makes it more difficult for the gland to produce hormone.

**Radioactive iodine treatment:** This treatment is commonly prescribed to people who have an overactive thyroid gland, a condition known as hyper thyroidism. However, radiation destroys the cells in the thyroid gland. this usually leads to hypo thyroidism.

**Use of certain medications:** Certain medicines to treat heart problems, psychiatric conditions and cancer can sometimes affect the production of thyroid hormone. These include amiodarone (cordarone, Pacerone), interferon alpha and interleukin-2.

**Thyroid surgery:** Surgery to remove the thyroid will lead to hypothyroidism. If only part of the thyroid is removed, the remaining gland may still be able to produce enough hormone for the body's needs.

**Too little iodine in the diet:** The thyroid needs iodine to produce thyroid hormone. Our body doesn't make iodine, so we need to get it through diet. Iodized table salt is rich in iodine. Other food sources of iodine include shellfish, salt water fish, eggs, dairy products and seaweed. Iodine deficiency is rare in the U.S.

**Pregnancy:** The reason isn't clear, but sometimes inflammation of the thyroid occurs after pregnancy. This is called postpartum thyroiditis. Women with this condition usually have a severe increase in thyroid hormone levels followed by a sharp drop in thyroid hormone production. Most women with postpartum thyroiditis will regain their normal thyroid function.

**Problems with the thyroid at birth:** Some babies may be born with a thyroid gland that did not develop correctly or does not work properly. This type of hypothyroidism is called congenital hypothyroidism. Most hospitals in the U.S. screen babies at birth for this disease.

**Pituitary gland damage or disorder:** Rarely, a problem with the pituitary gland can interfere with the production of thyroid hormone. The pituitary gland makes a hormone, called thyroid-stimulating hormone (TSH), which tells your thyroid how much hormone it should make and release.

**Disorder of the hypothalamus:** An extremely rare form of hypothyroidism can occur if the hypothalamus in the brain does not produce enough of a hormone called TRH. TRH affects the release of TSH from the pituitary gland.

Autoimmune thyroiditis is associated with other immune-mediated diseases such as diabetes mellitus type 1, pernicious anaemia, myasthenia gravis, celiac disease, rheumatoid arthritis and systemic lupus erythematosus. It may occur as part of autoimmune polyendocrine syndrome (type 1 and type 2).

### **Classes of Hypothyroidism**

Primary hypothyroidism is characterized by a high serum thyrotropin (TSH) concentration and low serum free thyroxine (T4) concentration, caused by a problem with the thyroid gland itself.<sup>6</sup> Subclinical hypothyroidism is defined biochemically as a normal free T4 concentration in the presence of an elevated TSH concentration. Other terms for this condition are mild hypothyroidism, early thyroid failure, preclinical hypothyroidism and decreased thyroid reserve.

Secondary (Central) hypothyroidism is characterized by a low serum T4 concentration and a serum TSH concentration that is not appropriately elevated. It occurs when another problem interferes with the thyroid's ability to produce hormones. For example, the pituitary gland or hypothalamus produce hormones that trigger the release of thyroid hormone. A problem with one of these glands can make our thyroid underactive.

Sometimes, an underactive thyroid that results from a problem with the hypothalamus is called tertiary hypothyroidism.

Transient or temporary hypothyroidism can be observed as a phase of subacute thyroiditis.

Consumptive hypothyroidism identified in an increasing number of clinical settings, is the result of accelerated inactivation of thyroid hormone by the type 3 iodothyronine deiodinase(D3).

## **EPIDEMIOLOGY:**

Accurate assessment of the prevalence and incidence of hypothyroidism is difficult due to variation in definitions and population samples. The prevalence of previously undiagnosed, spontaneous, hypothyroidism has been estimated to be between 2 and 4 per 1000 of the total population world wide. However, if all cases of previously diagnosed hypothyroidism and the effects of previous thyroid surgery and radioiodine treatment are included, this prevalence rises to approximately 10 per 1000. In the UK, primary hypothyroidism is common with a prevalence of 14/1000 women (but 1/1000 men). Despite these data, population screening for autoimmune hypothyroidism is thought to be probably not cost effective unless incorporated in to a screening programme for other conditions. Although the disease may occur at any age, most patients are between 30 and 60 years of age.<sup>7</sup>

## **DIAGNOSIS:**

Laboratory testing of thyroid stimulating hormone levels in the blood is considered the best initial test for hypothyroidism; a second TSH level is often obtained several weeks later for confirmation. Levels may be abnormal in the context of other illnesses, and TSH testing in hospitalized people is discouraged unless thyroid dysfunction is strongly suspected. An elevated TSH level indicates that the thyroid gland is not producing enough thyroid hormone, and free T4 levels are then often obtained. Measuring T3 is discouraged by the AACE in the assessment for hypothyroidism. There are a number of symptom rating scales for hypothyroidism; they provide a degree of objectivity but have limited use for diagnosis.<sup>8</sup>

Many cases of hypothyroidism are associated with mild elevations in creatine kinase and liver enzymes in the blood. They typically return to normal when hypothyroidism has been fully treated. Levels of cholesterol, low-density lipoprotein can be elevated; the impact of subclinical hypothyroidism on lipid parameters is less well-defined.

Very severe hypothyroidism and myxedema coma are characteristically associated with low sodium levels in the blood together with elevations in antidiuretic hormone, as well as acute worsening of kidney function due to a number of causes. In most cases, however, it is unclear if the relationship is casual.

A diagnosis of hypothyroidism without any lumps or masses felt within the thyroid gland does not require thyroid imaging; however, if the thyroid feels abnormal, diagnostic imaging is then recommended. The presence of antibodies against thyroid peroxidase (TPO) makes it more likely that thyroid nodules are caused by autoimmune thyroiditis, but if there is any doubt, a needle biopsy may be required.

Table :1: Level of Hypothyroidism :

TSH Thyroid stimulating hormone (0.4 mu/L)	T4 Thyroxine (4.6-12 ug/dl)	INTERPRETATION
Normal	Normal	Normal thyroid function
Elevated	Low	Overt hypothyroidism
Normal/Low	Low	Central hypothyroidism
Elevated	Normal	Subclinical hypothyroidism

**Central:**

If the TSH level is normal or low and serum free T4 levels are low, this is suggestive of central hypothyroidism (not enough TSH or TRH secretion by the pituitary gland or hypothalamus). There may be other features of hypopituitarism, such as menstrual cycle abnormalities and adrenal insufficiency. Central hypothyroidism should be investigated further to determine the underlying cause.

**Overt:**

In overt primary hypothyroidism, TSH levels are high and T4 and T3 levels are low. Overt hypothyroidism may also be diagnosed in those who have a TSH on multiple occasions of greater than 5 m IU/L, appropriate symptoms, and only a borderline low T4. It may also be diagnosed in those with a TSH of greater than 10 m IU/L.

**Sub clinical:**

Subclinical hypothyroidism is a milder form of hypothyroidism characterized by an elevated serum TSH level, but with a normal serum free thyroxine level. This milder form of hypothyroidism is most commonly caused by Hashimoto's thyroiditis. In adults, it is diagnosed when TSH levels are greater than 5ml U/L and less than 10ml U/L. The presentation of subclinical hypothyroidism is variable and classic signs and symptoms of hypothyroidism may not be observed. Of people with subclinical hypothyroidism, a proportion will develop overt hypothyroidism each year. In those with detectable antibodies against thyroid peroxidase (TPO), this occurs in 4.3 %, while in those with no detectable antibodies, this occurs in 2.6%. Those with subclinical hypothyroidism and detectable anti-TPO antibodies who do not require treatment should have repeat thyroid function tests more frequently (e.g. Yearly) compared with those who do not have detectable anti-TPO antibodies.

**Pregnancy:**

During pregnancy, the thyroid gland must produce 50% more thyroid hormone to provide enough thyroid hormone for the developing fetus and the expectant mother. In pregnancy, free thyroxine levels may be lower than anticipated due to increased binding to globulin and decreased binding to albumin. They should either be corrected for the stage of pregnancy, or total thyroxine

levels should be used instead of diagnosis. TSH values may also be lower than normal (particularly in the first trimester) and the normal range should be adjusted for the stage of pregnancy.

In pregnancy, subclinical hypothyroidism is defined as a TSH between 2.5 and 10 milli U/L with a normal thyroxine level, while those with TSH above 10 ml U/L are considered to be overtly hypothyroid even if the thyroxine level is normal. Antibodies against TPO may be important in making decisions about treatment, and should, therefore, be determined in women with abnormal thyroid function tests.

Determination of TPO antibodies may be considered as part of the assessment of recurrent miscarriage, as subtle thyroid dysfunction can be associated with pregnancy loss, but this recommendation is not universal, and presence of thyroid antibodies may not predict future outcome.

## **TREATMENT:**

By the end of the 19<sup>th</sup> century, myxedema had been attributed to diminished thyroid function and a cretinism like condition had been observed following thyroidectomy in animals and humans (Lindholm and Laurberg). Moreover, xeno transplantation of animal thyroid gland had been shown to improve symptoms in women suffering from myxedema temporarily. In 1891, Murray described the first regime of thyroid hormone replacement, subcutaneously injecting extract of sheep thyroid into a patient with hypothyroidism. It was soon shown that oral administration of thyroid extract was as effective. In 1914, Kendall purified thyroxine crystals, which became commercially available. Harrington identified the structure of thyroxine in 1926 and synthetic thyroxine was available for clinical use by the 1930s (Murray, 1891). However, it took many more years before thyroxine became preferable to desiccated thyroid extract as the treatment of choice for hypothyroidism (Fox, 1661). In 1952, Gross and Pitts-River identified the more potent liothyronine.<sup>9</sup>

The most common treatment is Levothyroxine (Levoxyl, Synthroid, Tirosint, Unithroid, Unithroid Direct), a man-made version of the thyroid hormone thyroxine (T4).

It should be given based on age, health, thyroid hormone levels, and body weight. 1.6 µg/kg/day is safe, effective, and requires fewer resources than using a more traditional approach of starting with a small dose and gradually raising the amount over time until we experience the effect. The exceptions to this are the elderly and patients with known ischemic heart disease.

It comes as a tablet to be taken by mouth on an empty stomach. Blood sugar levels are to be monitored regularly while taking this medication. Dietary fibre may decrease the absorption of this medication.

Thyroid hormone replacement is usually needed for life. If for any reason the medicine needs to be changed, it is important to have blood tests for TSH done again. Dose will be adjusted based

upon our TSH tests. Over time, doses of thyroid hormone that are too high can lead to bone loss, abnormal heart function, and abnormal heart rhythms. Doses that are too low may not relieve your symptoms. Dose adjustment may be necessary during pregnancy and at other times, and can be during regular check-ups with doctor.

**Contraindications:**

Levothyroxine is contraindicated in people with hypersensitivity to levothyroxine sodium or any component of the formulation, people with myocardial infarction, and people with thyrotoxicosis of any etiology.

Levothyroxine is also contraindicated for people with uncorrected adrenal insufficiency, as thyroid hormones may cause an acute adrenal crisis by increasing the metabolic clearance of glucocorticoids. For oral tablets the inability to swallow capsules serves as an additional contraindication.

**Combination therapy:**

The drug most commonly used to treat hypothyroidism is a type of T4 known as levothyroxine. A study published in December 2009 in the European Journal of Endocrinology evaluated quality of life, depression and anxiety rating scales and patient's preferences and concluded that a combination of T4/T3 (Levothyroxine and Triiodothyronine) is superior to treatment with only T4 (Levothyroxine) for hypothyroidism.<sup>10,11</sup>

**Natural Desiccated thyroid (NDT)**

NDT hormone is a drug derived from the dried glands of pigs. It is also called natural thyroid, thyroid extract, Procaine thyroid, pig thyroid, and known by brand names **Armour thyroid** and nature thyroid. It contains both thyroxine and triiodothyronine in a ratio of 4:1, there is no clinical trial evidence to show that it is more effective than levothyroxine.<sup>12</sup>

**Ayurvedic treatment:**

People suffering from hypothyroidism suffer from fatigue and hormonal imbalance. They need to concentrate on their diet and also need to ensure that they take their medications on time, if they want to get themselves completely cured.<sup>13</sup>

Ayurveda also states the following –

People suffering from hypothyroidism must consume milk.

These people are also asked to eat some specific vegetables like cucumber in large quantities to assist in treating hypothyroidism.

Pulses like moong dal and Bengal gram help in treating hypothyroidism.

Consume rice and barley.

Yoga helps in stabilising the thyroid gland, various asanas such as the sarvangasan and the suryanamaskar help the thyroid gland secret sufficient thyroid hormones.

Pranayama helps the thyroid gland in producing more of thyroid hormones.

Numerous herbs like the gokshura, brahmi, jatamansi and punarvana are used in ayurvedic treatment for hypothyroidism.

Hypothyroidism is caused due to the deficiency of iodine. Including foods that are high in iodine will help reduce the condition.

Mahayograjguggulu and ashwagandha are also used to treat this condition with ayurvedic treatment for hypothyroidism.

With proper treatment and with regular exercises along with a proper diet can help the people suffering from hypothyroidism get well soon. Remember our thyroid gland is very important for us to have a healthy long life. This condition is most common and thankfully there are several treatments available for the same. However, it is necessary that this condition must be treated in time since the failure of treating this problem may lead to other severe health complications for the person.

Do remember to take good care of ourselves in order to get good results of your treatment. Believe in our treatment and do all that our doctors ask us to do so that we can live a very happy and a healthy life for a long time to come.

### **HOMEOPATHIC TREATMENT:**

Homeopathy treats the person as a whole. This means that homeopathic treatment focuses on the patient as a person, as well as his pathological condition. The Homeopathic thyroid treatment medicines are selected after a full individualizing examination and case-analysis, which includes the medical history of the patient, physical and mental constitution etc. A miasmatic tendency (predisposition/susceptibility) is also often taken into account for the treatment of chronic conditions.<sup>14</sup>

Homeopathy offers good prognosis to cases of hypothyroidism. Homeopathic medicines like Calcarea phosph, Calcarea carb, Lapis alb, Iodium, Thyroidinum, Spongia, Lycopus, Calcarea iod, Ammonium carb, Graphites etc. are often found indicated in cases of hypothyroidism and thyroid dysfunction.

### **Complications:**

Hypothyroidism can lead to a number of health disorders if it is left untreated, some of the potential problems that may develop are listed here:<sup>15</sup>

- Myxoedema coma, Infertility, Miscarriage
- Impaired fertility, Difficulty in conceiving, Easy miscarriage
- Mental retardation , Cardiac diseases

- Lead to increased level of LDL, Psychological problems
- Rise of cardiomyopathy, Heart failure, Depression

## **CONCLUSION:**

Hypothyroidism is a disorder of the endocrine system in which thyroid gland does not produce enough thyroid hormone, which is readily diagnosed, Over the last decade, improvements have been made in laboratory tests to assess thyroid function, Coming to management it is potentially fatal if untreated, leads to different types of disorders that make the life discomfort or life threatening condition. Though it is not cured but can be treated by allopathic, ayurvedic and homeopathic methods. Management must be individualized based on many factors, including the etiology of the dysfunction, the attributes of the patient, the benefits and risks of treatment and available medication.

## **REFERENCE:**

1. Database of endocrineweb.com, Available from <https://www.healthline.com/human-body-maps/neck-organs/male#1>.
2. Database of endocrineweb.com <https://www.webmd.com/women/hypothyroidism-underactive-thyroid-symptoms-causes-treatments#3-5>.
3. Database of National Institute of Diabetes and Digestive and Kidney Diseases – NIH, <https://www.niddk.nih.gov/health-information/endocrine-diseases/hypothyroidism>.
4. Database of slideplayer.com, <http://slideplayer.com/slide/5107362/>.
5. Database of endocrineweb.com <https://medicaldictionary.thefreedictionary.com/hypothyroidism>.
6. Database of endocrineweb.com, <https://www.slideshare.net/vitrag24/hypothyroidism-13867948>.
7. Roger Walker – Clinical pharmacy and Therapeutics, Fourth edition, Thyroid and parathyroid disorders, page.no:671
8. Database of Wikipedia.org, <https://en.wikipedia.org/wiki/Hypothyroidism>
9. M Abid, Kapil kumar Sharma et.al., “Complication and Management of Hypothyroidism -A Review”, Indian Journal of Drugs, 2016,4(2),42-56.
10. Database of endocrineweb.com [https://www.medindia.net/doctors/drug\\_information/levothyroxine.html](https://www.medindia.net/doctors/drug_information/levothyroxine.html).
11. Database of endocrineweb.com <https://www.onlymyhealth.com/ayurvedic-treatment-hypothyroidism-1314094263>.

12. Database of partellpharmacy.com, <https://partellpharmacy.com/thyroid-hormone-t4-t3-combination-therapy/>.
13. Database of endocrineweb.com, <https://www.verywellhealth.com/levothyroxine-vs-combination-therapy-hypothyroidism-4571031>.
14. Database of welling homeopathy, <https://www.wellinghomeopathy.com/treatment-hypothyroid/>.
15. Database of endocrineweb.com, <https://www.endocrineweb.com/conditions/thyroid/hypothyroidism-too-little-thyroid-hormone>.
16. Database of endocrineweb.com <https://www.endocrineweb.com/conditions/hypothyroidism/how-doctors-diagnose-hypothyroidism>.
17. Database of endocrineweb.com <https://www.webmd.com/women/guide/low-thyroid-treatment#1>.
18. Database of endocrineweb.com <https://www.mayoclinic.org/diseases-conditions/hypothyroidism/diagnosis-treatment/drc-20350289>.
19. Database of Longdom publishing.com, <https://www.longdom.org/thyroid-disorders-therapy.html>.
20. Database of hormone.org, <http://www.harmones&you/patient-information-page-hypothyroidism>
21. American Thyroid Association: Hypothyroidism brochure. (2008) Available from [http://www.thyroid.org/patients/patient\\_brochures/hypothyroidism.html#causes](http://www.thyroid.org/patients/patient_brochures/hypothyroidism.html#causes).
22. Shah Kruti N, Gohil Priyanshee V et.al., Hypothyroidism and Atherosclerosis: From Etiology to Pathophysiology Scholars Academic Journal of Pharmacy (SAJP) Sch. Acad. J. Pharm., 2014; 3(1): 89-96
23. Shahid SB et al. "Subclinical Hypothyroidism and its Associated Disorders", Journal of Thyroid Disorders and Therapy, Shahid, Thyroid Disorders Ther 2018; 7:2
24. Layal Chaker, Antonio C Bianco et.al, Hypothyroidism, Lancet 2017; 390: 1550–62.
25. Jabbar, A. Yawar, A. Waseem, et.al. "Vitamin B12 deficiency common in primary hypothyroidism". JPMA. The Journal of the Pakistan Medical Association. 2008; 58(5): 258-61.
26. Jacob, H. and Peters, C. Screening, diagnosis and management of congenital hypothyroidism: European Society for Paediatric Endocrinology Consensus Guideline. Arch. Dis Child. Educ. Pract. Ed. 2015; 100 (5): 260-3.

27. Laurberg P. Global or Gaelic epidemic of hypothyroidism. *The Lancet*. 2005; 365(9461): 738740.
28. Leese, G.P. Flynn, R.V. Jung, R.T. Macdonald, T.M. Murphy, M.J. and Morris, A.D. Increasing prevalence and incidence of thyroid disease in Tayside. *Clin. Endocrinol (Oxf)*, 2008; 68(2), 311-6.
29. Lin, C.C. Chen, T.W. Ng, Y.Y. Chou, Y.H. and Yang, W.C. Thyroid dysfunction and nodular goiter in hemodialysis and peritoneal dialysis patients. *Perit. Dial. Int.*, 1998; 18(5): 51621.16
30. Lindholm, J. and Laurberg, P. Hypothyroidism and thyroid substitution: historical aspects. *J Thyroid Res.*, 2011; 1-10.
31. Loeber, G. Webseter, D. Anaraze, A Quality evaluation of neonatal screening program. *Acta. paediatric. supply*, 1999; 88: 3-6.