Case Report

Indian Journal of Genetics and Molecular Research
Volume 10 Number 1, January–June 2021
DOI: http://dx.doi.org/10.21088/ijgmr.2319.4782.10121.3

Case Study on Under-Activethyroid and its Associated Ailments

Nadia Naseer[1], V Venugopal Rao[2]

How to cite this article:
Nadia Naseer, V Venugopal Rao/Case Study on Under-Activethyroid and its Associated Ailments/Indian J Genet Mol Res. 2021;10(1):21–25.

Abstract

The purpose behind this case study is to examine the function of thyroid gland, understand the regulation of thyroid hormones, to correlate the symptoms with respect to thyroid dysfunction and its associated consequencesfollowed by clinical interventionsand the pharmaceutical care plan. A female patient with an age of 48 years old is suffering from hypothyroidism and was followed up, information was collected and analyzed.

Pedigree analysis revealed that there is an important component of genetics in causation of disease and is reflected to be due to consanguineous marriages in previous generations of the patient which must have added the risk over general population, another consideration is the occurrence affected relatives who are third degree relatedand can support in the genetic component of the disease.

Keywords: Hypothyroidism; Hashimoto's thyroiditis; Antithyroid antibodies; Autoimmune disorder.

Introduction

Thyroid gland is a part of the body's endocrine system, it is present below the larynx on either sides of the anterior trachea. It is also a largest organwith destined with special endocrine function in human body, normally weighing 15 to 20 grams in adults and is necessary to normal body growth in infancy and childhood. The thyroid gland secretes two major hormones thyroxine (T3)and triiodothyronine (T4), and the Thyroid secretion is controlled by thyroid stimulating hormone (TSH), which is secreted by anterior pituitary gland.

Thyroid hormones synthesis involves Thyroidal peroxidase (TPO) which causes (a) oxidation of Iodine to Di-iodine in presence of H2O2, (b) iodination of tyrosyl residues in thyroglobulin, (c) coupling of MIT and DIT by a process called as Iodine-organification .

Types of Thyroid Disorders

Based on the levels of thyroid hormones they are classified into two types:

- *Hypothyroidism:* Hypothyroidism is a clinical syndrome resulting from deficiency of thyroid hormones due to their insufficient synthesis which in turn results in a generalized slowing down of metabolic processes.[1], It is sometimes referred as 'Silent disease'.
- The clinical manifestations of Hypothyroidism, depending upon the age at onset of disorder are divided into two types – Cretinism (in infants and children) and Myxedema (in adulthood). Two principal types of Hypothyroidism are Primary Hypothyroidism and Secondary Hypothyroidism.
- *Hyperthyroidism:* Hyperthyroidism, also called overactive thyroid, it is a condition when the thyroid gland makes more or excessive thyroid hormones than your body needs. It is characterized by normal or high thyroid radioactive iodine uptake (thyrotoxicosis with hyperthyroidism or true hyperthyroidism).

The most common cause of hyperthyroidism is

Author's Affiliation: [1]Student Genetics, [2]HOD of genetics Department, Department of Genetics, St Ann's College for Women, Mehdipatnam, Hyderabad, Telangana 500028, India.

Corresponding Author: V Venugopal Rao, HOD of genetics Department, St Ann's College for Women, Mehdipatnam, Hyderabad, Telangana 500028, India.

E-mail: rao5749@gmail.com

Graves' disease, followed by toxic nodular goiter. Hyperthyroidism can be overt or subclinical. Overt hyperthyroidism is characterized by low serum thyroid-stimulating hormone (TSH) concentrations and raised serum concentrations of thyroid hormones: thyroxine (T4), triiodothyronine (T3), or both. Subclinical hyperthyroidism is characterized by low serum TSH, but normal serum T4 and T3 concentrations.

Table 1: Levels in Hypothyroidism and Hyperthyroidism.

	Hypothyroidism	Hyperthyroidism
TSH levels	High	Low
T3 and T4 levels	Low	High

Heritability of Thyroid Hormones

It has been recognized for some time that circulating TSH, free thyroxine (free T4) and free triiodothyronine (free T3) concentrations in euthyroid individuals have a much greater inter-individual than intra-individual variation.

Several studies have attempted to estimate the genetic and environmentalcontribution to this individual set point using either twin and familybased study designs.Studies on the heritability of thyroid function have provided wide ranging estimates.[2-3]

Gene involved in central hypothyroidism

TSHR

It is the most commonly mutated gene in thyroid dysfunction however, mutations in this gene are associated with a variable resistance to TSH. The severity depends on the type of mutation and the number of mutated TSHR alleles. If TSH resistance is partial, patients exhibited Euthyroid.

Types of Hypothyroidism

Conditions that can cause hypothyroidism include:

- Primary hypothyroidism
- Central hypothyroidism

Clinical Findings

Slowing of metabolic processes

Signs include: Slow movement and slow speech, Delayed relaxation of tendon reflexes, Bradycardia, Carotenemia.

Symptoms include: Fatigue and weakness, Cold intolerance, Dyspnea on exertion, Weight gain, Cognitive dysfunction, Mental retardation, Constipation, Growth failure.

Accumulation of matrix substances

Signs include: Coarse skin, Puffy face and loss of eyebrows, edemaEnlargement of the tongue.

Symptoms include:Dry skin, Hoarseness, Edema

Other

Signs include: Diastolic hypertension, Pleural and pericardial effusions, Galactorrhea.

Symptoms include: Decreases hearing, Myalgia and paresthesia, Depression, pubertal delay.

Pathophysiology and associated factors

Iron deficiency associated with hypothyroidism

Metabolism of thyroid hormones and iron is interdependent,insufficient or deficiency of iron can result in hypothyroidism and vice versa.Iron metabolism is very intricately connected to thyroid hormone metabolism.

Normal thyroid status is dependent on the presence of many trace elements e.g., iron, iodine, selenium, and zinc for both the synthesis and metabolism of thyroid hormones.[4] Iron is a component of many enzymes including thyroid peroxidase (TPO) which takes part in the initial two steps in thyroid hormone biosynthesis.[5] Low ferritin levels have also been observed in hypothyroid patients.[6]

Several studies in animals and humans have shown that nutritional iron deficiency may significantly lower the circulating levels of both thyroxine and triiodothyronine and may also reduce conversion of T4 to T3.[7-8] Alterations in thyroid status produce changes in serum ferritin levels.

Symptoms like anxiety, brittle nails, poor short term memory, restless, dizziness, palpitations, irregular heartbeats may be seen in patients who are 5 under treatment with thyroxine and are iron deficient.

Folate deficiency associated with hypothyroidism Folate, or folic acid, is an essential B vitamin that is needed for the proper formation of red blood cells and their division and DNA synthesis. This vitamin shares an important, but somewhat indirect relationship with a condition known as hypothyroidism. In this condition patients does not get adequate amount folate in the diet and are mostly found to have increased risk for heart disease.

Prevalence of vitamin B12 deficiency increases along with the age. Patients with deficiency of vitamin.

B12 and hypothyroidism usually have symptoms of fatigue, weakness, poor memory retention, itchingand loss of sensation.[9]

Folic acid or vitamin B12 deficiency is due to impaired intestinal absorption, macrocytic anemia associated in hypothyroidism. Folate deficiency is mainly due to low intake of greens leafy vegetables, legumes and meat.

It has been reported that, folate prevents degeneration of neurons in adults and also improves cognitivefunctions and decreasesdepression.[10,11] Vitamin B12 deficiency may also cause a decrease in folate level because of the available methyl tetrahydrofolate (MTHF)is not utilized due to folate trap.

Diagnosis and Management

Serum TSH levels profile is used to screen for hypothyroidism in patients whose TSH levels are elevated and free T4 levels are normal. TSH produced can be biologically inactive and can affect the levels of bioactive TSH, hence the diagnosis of hypothyroidism is based on free T4 and TSH.

Method of Diagnosis: Chemo-luminescence Immuno Assay (CLIA).

Hypothyroidism has clinical implications such as Anemia, hypertension, iron deficiency and folate deficiency this is found to be a pleiotropic effect of the thyroid hormone which can also result in other disorders that can be a long-term consequence.

Levothyroxine mono-therapy is the standard treatment for hypothyroidism which can significantly decrease serum lipids and decrease body mass, thus improving clinical features of metabolic syndrome.

Case Study

Objective: The main objective of this study is to throw light on genetic aspects while studying clinical manifestations.

A patient aged 48 suffering from hypothyroidism for the last 41 years with age at onsetof 7 yearswas followed up for clinical investigations confirming that she is a case of under-active thyroid.

Laboratory readings includes

Vital Physical Examination

Parameters	Reported Value	Normal Value
Pulse rate	85	70-90 /min
Respiratory rate	29	18-30 /min

Biological and Pathological Examination

Parameters	Reported Value	Normal Value
T3	0.93	0.6-1.81ng/mL
T4	6.50	3.2-12.6 ng/mL
TSH	26.47	0.35-5.5

Comments (or)Interpretations show that:

- TSH levels are increased in primary Hypothyroidism.
- Increase in TSH and Decrease in T3 & T4 leads to Overt Hypothyroidism.

Sign and Symptoms

Symptoms observed in patient includes Fatigue,Tiredness, sensitivity towards cold, muscle and join aches, puffed face, dull facial expression, swelling in neck region, voice changes,dry and scaly skin and constipation, Symptomsof Anxiety, depression, psychosis, cognitive impairment such as memory loss is also present.

Pharmaceutical Care Plan

Drug

(Levothyroxine Sodium)

Therapy: Levothyroxine treatment therapy

Category: Synthetic Thyroid Hormone.

Toxicity parameters: Sleep problems (Insomnia), Nervousness.

Mechanism: Pharmacokinetic, Absorption.

Management should be administered one hour before or two hours after meals.

Drug name	Category	Dose
Levothyroxine	Thyroxine hormone	100mg
Syp-Zincovit	Vitamin and mineral supplement	5ml

Patient counseling

Patient was told to eat nutritious and maintain balanced diet, avoid taking caffeine and processed food, and was also said to reduce the intake of dairy products and was strictly said to avoid Iodized food because iodine increases the activity of thyroid gland and may result in goiter development.

Patient was suggested to consume moreVitamin B12, vitamin C and Vitamin E in diets as they have antioxidant properties that are beneficial in deactivating the harmful effects of free radicals that can lead to severity in hypothyroidism.

Result

The patient has family history with three degree of relatives affected with hypothyroidism, the common symptoms accounted are sensitivity to cold and constipation. Rare symptoms include snoring, hoarse voice. The patient does not have goiter to explain oropharyngeal symptoms. The biochemical findings were normal and could only interpret the decrease of T3 and T4 levels with elevated increase in TSH level.

Pedigree Analysis

(MSD: mother's sister's daughter, MBD: mother's brother's daughter) referred to as consanguineous marriage.

Affected Relatives in the pedigree

- Paternal and Maternal grandmother has one affected brother. (Paternal and maternal grandmother are sisters and they both have same brother).

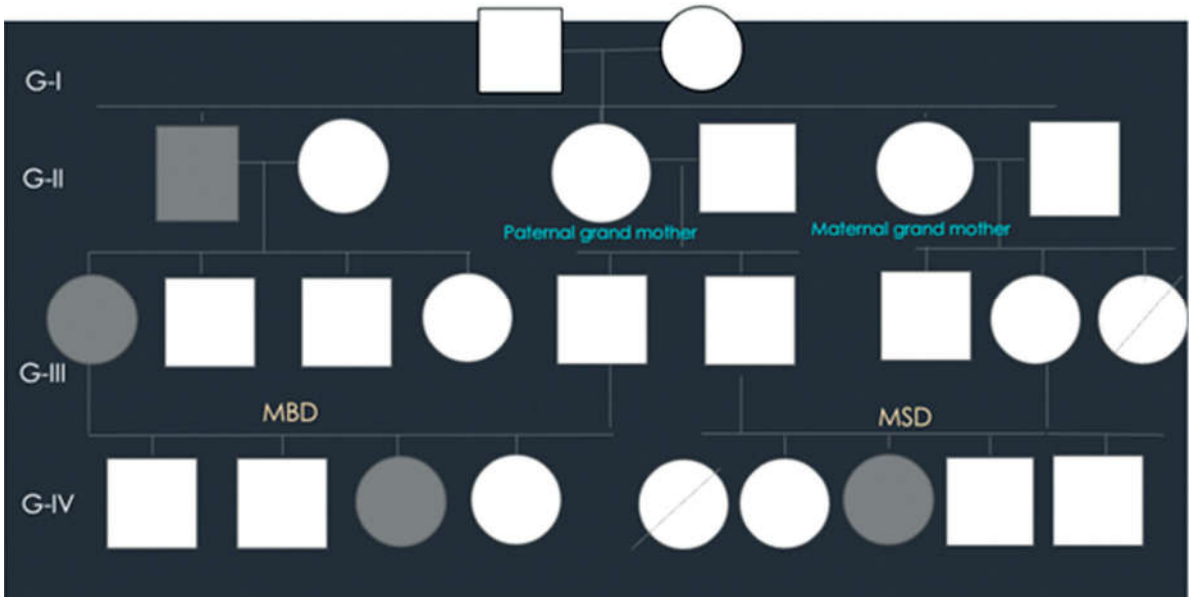

Fig. 9: Pedigree showing affected individuals with hypothyroidism.

- Paternal uncles wife is affected. (Paternal uncles wife is married within family and is a blood relative).

Degree of relatives with hypothyroidism

- 3rddegree relative: Paternal uncles wife (III-1)
- 3rd degree relative: Paternal-First cousin sister (IV-3).
- 3rd degree Grand uncle (II-1).

(siblingto paternal and maternal grandmother also fatherof paternal uncles wife).

Conclusion

The aim of this case study was to study the association between thyroid hormones and underlying conditions, genetic and environmental in manifestation of clinical symptoms.

However pedigree analysis revealed that there is an important component of genetics in causation of disease as is reflected by consanguineous marriages in previous generations of the patient which must have added the risk over general population. Another consideration is the occurrence affected relatives who are third degree and supports in contributing the genetic component of the disease.

Further investigations are however necessary to identify molecular biomarkers associated with thyroidism and their inheritance to future generations.

Refrences

1. Hypothyroidism — A silent phenomenon. Rai Amit kumar, Deepshika. Wjpr.net 2015; 6; 664-676.
2. Panicker V, Wilson SG, Spector TD, Brown SJ, Falchi M, Richards JB, et al. Heritability of serum TSH, free T4 and free T3 concentrations: a study of a large UK twin cohort. Clin Endocrinol (Oxf) 2008;68:6529. [PubMed] [Google Scholar]
3. Hansen PS, Brix TH, Sørensen TI, Kyvik KO, Hegedüs L. Major genetic influence on the regulation of the pituitary-thyroid axis: a study

of healthy Danish twins. J Clin Endocrinol Metab. 2004;89:11817.[PubMed] [Google Scholar].

4. Das C, Sahana PK, Sengupta N, Giri D, Roy M, Mukhopadhyay P. Etiology of anemia in primary hypothyroid subjects in a tertiary care center in Eastern India. Indian J EndocrMetab 2012; 16, Suppl S2:361-363.
5. Metwalley KA, Farghaly HS, Hassan AF. Thyroid status in Egyptian primary school children with iron deficiency anemia: Relationship to intellectual function. Thyroid Res Pract 2013; 10: 91-5.
6. Sonja YH, Michael BZ, Myrtha A, Wolfgang L, Richard FH. Iron deficiency anemia reduces thyroid peroxidase activity in rats. J Nutrition 2002; 132: 1951-1955.
7. Shakir KM, Turton D, Aprill BS, Drake AJ, Eisold JF. Anemia: a cause of intolerance to thyroxine sodium. Mayo Clinic Proceedings 2000; 75: 189-192.
8. Chen SCH, Shirazi MRS, Orr RA. Triiodothyronine and thyroxine levels in iron deficient, hyper triglyceridemic rats. Nutr Res 1983; 3: 91-106. Beard JL, Borel MJ, Deer J. Impaired thermoregulation and thyroid function in iron deficiency anemia. Am J ClinNutr 1990; 52: 813-819.
9. Snow CF. Laboratory diagnosis of vitamin B12 deficiency. Arch Inter Medicine 1999; 159; 1289-98.
10. Zhuo JM, Pratico D, Acceleration of brain amyloidosis in an Alzheimer's disease mouse model by a folate, vitamin B6 andB12-deficient diet, Exp Gerontol, 45 (3), 2010, 195-201.
11. Beydoun MA, Fanelli Kuczmarski MT, Beydoun HA, Shroff MR, Mason MA, Evans MK, Zonderman AB, The sex-specific role of plasma folate in mediating the association of dietary quality with depressive symptoms, J Nutr, 2010; 140(2), 338-347.