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Subclinical hypothyroidism

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Abstract

Overt hypothyroidism is characterized by elevated values of thyroid-stimulating hormone (TSH) in the presence of low thyroid-stimulating hormone (FT4). In contrast, subclinical hypothyroidism is characterized by elevated TSH values in the presence of normal levels of circulating FT4. In the general population, the upper limit of a normal TSH level is usually reported to be about 4.5 mL/L, based on the distribution of TSH levels in a disease-free population with normal thyroid function. The aim of this article is to identify subclinical hypothyroidism across age groups. Several studies in the past few years have indicated that treating subclinical hypothyroidism in older adults does not actually affect thyroid-related symptoms or quality of life. An increasing number of researchers are arguing that older adults are being overdiagnosed with subclinical hypothyroidism and that there is usually no need to treat slightly elevated TSH levels in adults older than 65 years. It is therefore well established that TSH levels tend to be lower in younger individuals and higher in older adults.

Key words: Subclinical hypothyroidism, thyroid-stimulating hormone, TSH, FT4.

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1. Background and Research Problem

Subclinical hypothyroidism is a biochemical condition where thyroid stimulating hormone (TSH) serum levels are above the upper limit of the reference range for the assay, whereas free thyroxine (FT4) values are within the reference interval of the assay. This condition is also known as isolated hyperthyrotropinemia or compensated hypothyroidism. Its importance rises from the potential progression to overt hypothyroidism and the fear of adverse complications. (1)

Subclinical hypothyroidism (SCH) is defined by elevated TSH (thyroid stimulating hormone) values and normal levels of free thyroid hormone (FT4). Among the diseases of the thyroid gland, this disorder remains elusive and may affect about 1-11% of the world's population. This wide variation can be attributed to environmental/ethnic characteristics, but it is noteworthy that it may also arise in the reference range for TSH used to determine the presence of abnormal thyroid function which is still actively debated, especially among countries. The prevalence of thyroid disease diagnoses increases with age and is the most common thyroid dysfunction in older persons, reaching 14.5% in individuals under 60 years and up to 22% in women over 60 years. This disorder has always been particularly difficult to identify because clinical signs may be present but are not necessarily related to biological indicators. Virtually no progress has been made in

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the diagnosis of SCH during the recent past although the pathology may be more detrimental with age. Recently, treatment with L-thyroxine in subjects over 65 years of age with SCH failed to demonstrate efficacy, suggesting that the distribution of age groups according to clinical signs related to hypothyroidism (hCS) and TSH level may not be sufficient. The research problem therefore lies in the identification of subclinical hypothyroidism across age groups:

2. Research Objectives

The main objective of this article is: "To identify subclinical hypothyroidism across age groups."

This main objective is subdivided into the following sub-objectives:

1) To define subclinical hypothyroidism.
2) To identify the causes of the prevalence of subclinical hypothyroidism across age groups.
3) To identify the criteria for case-finding in patients at risk of developing thyroid disease.
4) To identify the ways of diagnosing subclinical hypothyroidism across age groups.
5) To identify the ways to treat hypothyroidism, taking into account the age of the patient.

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3. Literature review

3.1 Subclinical hypothyroidism in non-pregnant adult

Subclinical hypothyroidism is a biochemical condition where the thyroid stimulating hormone (TSH) level is elevated above the normal reference range for the assay and free thyroxine (FT4) is normal. Subclinical hypothyroidism can be classified as mild when the TSH level is between 4.5 mU/L and 10 mU/L and severe when the TSH level above or equal 10mU/L. (1) The prevalence of subclinical hypothyroidism ranges from 4%-20% according to different studies. The prevalence is higher in women, white people, patients with thyroid autoimmunity, increasing age and iodine -sufficient areas. (2)

The etiology of subclinical hypothyroidism is similar to overt hypothyroidism with the most common cause worldwide is iodine deficiency, however in iodine sufficient areas the most common cause is Hashimoto's thyroiditis, other causes include suboptimal treatment of hypothyroidism, thyroidectomy, radioactive iodine treatment, external radiation, infiltrative disorders like Sarciodosis and drugs like amiodarone and Lithium). (2,3)

There is no clear evidence for routine screening of thyroid disease in adults, however various professional societies adopted different criteria for case finding in patients at risk of thyroid disease, the American Thyroid Association guidelines recommends starting screening at the age of 35 and to be repeated every five

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years in patients with no signs or symptoms of hypothyroidism and more frequently in patient how do have signs and symptoms. (2) Majority of patients with subclinical hypothyroidism have no symptoms, but common symptoms of subclinical hypothyroidism include Dry skin, cold intolerance, easy fatigability, coarse hair and constipation. (4)

The diagnosis of subclinical hypothyroidism is not made by a single laboratory test, the test should be repeated after one to three months, except in pregnant women or women planning to get pregnant. other causes of elevated TFT should be ruled out like the nocturnal measurement of TFT, recovery phase of nonthyroidal illness, hypothyroid phase of thyroiditis, assay variability or interference and central hypothyroidism before the diagnoses of subclinical hypothyroidism is made. (1) Subclinical hypothyroidism can progress to overt hypothyroidism in 33% to 55% within 10-20 years; the risk to progression is higher in patient with an initial TSH level exceeding 10 mU/L or elevated levels of thyroid peroxidase antibodies. Other risk factors for progression to hypothyroidism include female sex, older age, goiter, neck irradiation or radioactive iodine exposure, and high iodine intake. In patients with TSH levels below 10 mU/L and patients with negative thyroid peroxidase antibodies subclinical hypothyroidism tends to resolve. (1.2) Patients with subclinical hypothyroidism are at increased risk of myocardial infarction, cardiovascular disease and mortality, altered lipid profiles, stroke (in patients less than 65 of age), worsening of preexisting depression and bipolar disease, also the subclinical hypothyroidism may affect

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cognition. The increased cardiovascular risk is seen in patients with TSH level 7 mU/l or higher, the risk is higher with higher TSH levels. (1,2,5) Studies showed that Treatment of subclinical hypothyroidism decreased the cardiovascular risk and mortality in patients below 65 of age and it may improve mood, anxiety, cognition in older patients. (1,2)

Treatment of hypothyroidism is usually tailored according to the patient condition taking in the consideration patient age, sex, family history of thyroid disease, personal history of thyroid disease or autoimmune disease, clinical symptoms, cardiovascular risk, TSH level and the presence of thyroid peroxidase antibodies.

Both the American Thyroid Association (ATA) and American Association of Clinical Endocrinology (AACE) recommend starting levothyroxine therapy if the patient has any of the following: TSH >10 mU/l, hypothyroidism symptoms, cardiovascular risk factors or Positive thyroid peroxidase antibodies. (5)

For subclinical hypothyroidism with TSH level below 10 mU/l the treatment is still controversial, however, early treatment of patient with subclinical hypothyroidism and TSH level above 8 mU/l should be considered as the risk of progress to overt hypothyroidism is high.In milder forms of subclinical hypothyroidism a wait and see approach is recommended. (6)

Because of the minimal effect of the thyroid hormone deficiency the initial dose may be started at 25 mcg to 50 mcg daily dose of levothyroxine, the TSH level should be checked and the dose be adjusted every six to eight weeks until normalization of the TSH, once the TSH is in the target range the TSH monitoring

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intervals can be extended to every six to twelve weeks .not only the TSH level should be monitored the subclinical hypothyroidism symptoms should be also assessed after starting treatment ,if symptoms persists after treatment other causes should be considered .(4,6). Over treatment of subclinical hypothyroidism causes the TSH to be below the normal range that may result in hyperthyroidism symptoms like tiredness, weight loss, and restlessness as well as increased cardiac risk, and atrial fibrillation, other potential complications include low bone density and increase the risk of fracture. (1,6)

3.2 SCH in pregnancy

During pregnancy the metabolic rate increases, and this is reflected by the lower normal TSH levels compared to nonpregnant adults thought the pregnancy. the largest decrease is observed in the first trimester then it gradually rises in the second and third trimester. (7) Subclinical hypothyroidism in pregnancy is defines as an elevated TSH level above the population-based trimester specific reference ranges with normal Free thyroxine (T4) levels, when these reference ranges are not available ATA recommends to the TSH upper normal level of 4 mU/L.(7) The prevalence of subclinical hypothyroidism has been reported in 1.5% -5% of pregnancies in different studies (8).

Subclinical hypothyroidism in pregnancy is associated with pregnancy loss, placental abruption, gestational diabetes, gestational hypertension, eclampsia, premature rupture of membranes, preterm delivery and intrauterine growth

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retardation. Offspring of these pregnant ladies are more likely to be admitted in the neonatal intensive care unit. Subclinical hypothyroidism in pregnancy is also associated with low birth weight and it may be associated with negative impact on neurocognitive function of the offspring. (9)

Universal Screening of pregnant ladies for thyroid dysfunction is controversial, ATA recommends screening for ladies planning assisted reproduction or those known to have positive thyroid peroxidase antibodies prior to conception. ATA also recommends to screen patients seeking pregnancy or newly pregnant with high risk factors ,these factors include age above 30,morbid obesity, history of hypothyroidism or hyperthyroidism, presence of sign and symptoms of hypothyroidism, history of thyroid surgery ,presence of goiter , thyroid antibody positivity ,type 1 diabetes and other autoimmune disease , family history of autoimmune thyroid disease , history of head and neck radiation , ,history of pregnancy loss ,history preterm delivery , multiple prior pregnancies, use of amiodarone or lithium and residing in areas with known moderate to severe iodine insufficiency and.(7).

According to ATA guidelines treatment of subclinical hypothyroidism depends on TSH level and thyroid peroxidase antibodies presence. For thyroid peroxidase antibodies positive women and TSH level above the pregnancy- specific upper normal range (above 4 mU/L if unavailable) the treatment is strongly recommended, for thyroid peroxidase antibodies positive and the TSH level is between 2.5 mU/L and the upper normal range the treatment may be considered.

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For thyroid peroxidase antibodies negative women treatment is strongly recommended if the TSH level is higher than or equal to 10 mU/L,if the TSH level is above the pregnancy- specific upper normal range and below 10 mU/L treatment may be considered ,treatment is not recommended for TSH is between 2.5 mU/L and upper normal range .(7) There is no recommendation regarding the starting dose of levothyroxine, however starting with 50 mcg and then titrating according to TSH is advised. ATA recommends maintaining a TSH level below 2.5 mU/L. follow up every four to six weeks is advised. (7,9)

3.3 Subclinical hypothyroidism in children and adolescents

Thyroid hormones play a major role in growth regulation, bone maturation, puberty, body metabolism and brain maturation and function. In hypothyroidism these functions are impaired, and this is particularly important in children as there are in the growing and development stage. Subclinical hypothyroidism in children and adolescents is less common than in adults, it occurs in less than 3% of children and adolescents. (10)

The etiology of subclinical can be thyroidal that include Hashimoto's thyroiditis which is the most frequent cause and iodine deficiency or non-thyroidal that include diabetes mellitus, cystic fibrosis, celiac disease, chronic renal failure, and many syndromes, such as Turner, Down, Klinefelter, and Williams syndrome. Idiopathic subclinical hypothyroidism is subclinical hypothyroidism where no overt cause could be detected. (11) Subclinical hypothyroidism in children may not be always asymptomatic. Cardiovascular abnormalities and proatherogenic metabolic

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alterations were observed in a limited number of cases with long standing subclinical hypothyroidism. (12)

The progression to overt hypothyroidism largely depends on the underlying cause, Idiopathic subclinical hypothyroidism is generally benign with self-remitting course and low risk of progression to overt hypothyroidism while the subclinical hypothyroidism with clear underlying disease (more with autoimmune diseases) predicts more deteriorating of thyroid function especially if combined with TSH above 10 mU/L or if it coexisted with of either Turner syndrome or Down's syndrome. (10,12) Due to limited evidence, many factors should be considered before starting treatment of subclinical hypothyroidism in children like TSH level and its progression over time, underlying cause, presence of signs and symptoms of hypothyroidism and the associated diseases.

For patients of TSH 10 mU/L and more there is a general agreement on treatment by levothyroxine. For children with Hashimoto's thyroiditis -related subclinical hypothyroidism and progressive deterioration of thyroid status over time, particularly in the cases with associated Turner syndrome or Down's syndrome and/or other autoimmune diseases treatment should be recommended. Treatment might also be recommended for the children with goiter and hypothyroid signs or symptoms and/or proatherogenic metabolic abnormalities. (11) For children with mild persistent elevation of TSH and no thyroid replacement therapy a TSH monitoring every six months is advised, and when the TSH is stable for two years the interval between monitoring can be extended. (11)

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4. Conclusion

In conclusion, subclinical hypothyroidism is an early, mild form of hypothyroidism, a condition in which the body does not produce enough thyroid hormones. It is called subclinical because the level of serum thyroid-stimulating hormone only from the front of the pituitary gland is slightly higher than normal. Subclinical hypothyroidism is called "hidden", because the disease has no obvious symptoms. This form is the initial stage of the disease and is characterized by the defeat of the normal functioning of the thyroid gland. The disease is detected by analysis, in which the level of TSH will be significantly exceeded. Studies have shown that about 20% of women over 50 suffer from this disease, but the disease can develop at a younger age, even in children. Finally, it may be useful to emphasize that the movement toward a watch-and-wait approach for mild TSH elevations is particularly applicable to the elderly. In younger adults, damage from mild elevations is more pronounced, and treatment should be started sooner. However, lower sensitivity to hCS and changing levels of TSH with age make the diagnosis of SCH difficult in older individuals. An age-related reference range and/or development of assays capable of measuring bioactive TSH are required to improve detection of SCH in the elderly.

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www.mecsj.com/ar/

References

1- Tng EL. The debate on treating subclinical hypothyroidism. *Singapore Med J*. 2016;57(10):539-545. doi:10.11622/smedj.2016165 {PubMed}

2-Azim S, Nasr C. Subclinical hypothyroidism: When to treat [published correction appears in Cleve Clin J Med. 2019 Jun;86:392]. *Cleve Clin J Med*. 2019;86(2):101-110. doi:10.3949/ccjm.86a.17053 {PubMed}

3- Gosi SKY, Garla VV. Subclinical Hypothyroidism. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; July 15, 2021. {PubMed}

4- Adlin V. Subclinical hypothyroidism: deciding when to treat. *Am Fam Physician*. 1998;57(4):776-780 {PubMed}

5- Jasim S, Abdi H, Gharib H, Biondi B. A Clinical Debate: Subclinical Hypothyroidism. *Int J Endocrinol Metab*. 2021;19(3):e115948. Published 2021 Jul 24. doi:10.5812/ijem.115948 {PubMed}

6-Calissendorff J, Falhammar H. To Treat or Not to Treat Subclinical Hypothyroidism, What Is the Evidence?. *Medicina (Kaunas)*. 2020;56(1):40. Published 2020 Jan 19. doi:10.3390/medicina56010040{PubMed}

7- Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, Grobman WA, Laurberg P, Lazarus JH, Mandel SJ, Peeters RP, Sullivan S. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid. 2017 Mar;27(3):315-389.

doi: 10.1089/thy.2016.0457. Erratum in: Thyroid. 2017 Sep;27(9):1212. PMID: 28056690 {PubMed}

8- López-Muñoz E, Mateos-Sánchez L, Mejía-Terrazas GE, Bedwell-Cordero SE. Hypothyroidism and isolated hypothyroxinemia in pregnancy, from physiology to the clinic. Taiwan J Obstet Gynecol. 2019;58(6):757-763. doi:10.1016/j.tjog.2019.09.005 {PubMed}

9- Maraka S, Singh Ospina NM, Mastorakos G, O'Keeffe DT. Subclinical Hypothyroidism in Women Planning Conception and During Pregnancy: Who Should Be Treated and How?. *J Endocr Soc*. 2018;2(6):533-546. Published 2018 May 3. doi:10.1210/js.2018-00090 {PubMed}

10-Murillo-Vallés, M., Martinez, S., Aguilar-Riera, C. et al. Subclinical hypothyroidism in childhood, treatment or only follow-up?. BMC Pediatr 20, 282 (2020). https://doi.org/10.1186/s12887-020-02177-8

11-Crisafulli G, Aversa T, Zirilli G, et al. Subclinical Hypothyroidism in Children: When a Replacement Hormonal Treatment Might Be Advisable. Front Endocrinol (Lausanne). 2019;10:109. Published 2019 Feb 25. doi:10.3389/fendo.2019.00109 {PubMed}

12-Gallizzi R, Crisafulli C, Aversa T, et al. Subclinical hypothyroidism in children: is it always subclinical?. *Ital J Pediatr*. 2018;44(1):25. Published 2018 Feb 17. doi:10.1186/s13052-018-0462-4.