Review Article

Hypothyroidism in Elderly Population: A Review

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ABSTRACT

Many metabolic disorders originate from thyroid disorders, particularly from hypothyroidism. Hypothyroidism commonly occurs in elderly subjects, particularly in women. Subclinical form of hypothyroidism can be diagnosed via laboratory testing. It is crucial to check thyroid hormone profile in elderly subjects. Subclinical hypothyroidism can eventually lead to overt hypothyroidism if left untreated. Treatment of subclinical hypothyroidism could be helpful in preventing the complications of hypothyroidism, particularly among the elderly population. The main aim of this review was to investigate subclinical hypothyroidism among elderly subjects.

KEYWORDS: Hypothyroidism, Subclinical hypothyroidism, Elderly

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INTRODUCTION

Many metabolic disorders originate from thyroid disorders, particularly from hypothyroidism in which serum level of thyroid hormones are decreased. This condition mainly occurs in older women. In the subclinical form of hypothyroidism, clinical manifestations of thyroid disorders are not evident. However, this condition can be diagnosed through laboratory measurement of thyroid stimulating hormone (TSH) and thyroid hormonesthyroxine or tetraidothyronine (T4) and triidothyronine (T3). TSH is a pituitary hormone that stimulates thyroid gland to produce T4 and T3. In subclinical hypothyroidism, thyroid hormones are in normal range but the serum TSH is elevated.

In some clinical settings, subclinical hypothyroidism is treated as overt hypothyroidism since it is believed to be the pre-condition for hypothyroidism [1-19]. Thyroid disease may be sometimes missed in the elderly population because of the similarities between thyroid hormones-related clinical manifestation and normal aging physiological changes. Therefore, it is important to evaluate thyroid hormone profile in the elderly via laboratory testing to prevent the possible misdiagnosis and mistreatment.

Thyroid hormones abnormalities are common with increasing age, particularly among women. However, there are some reports indicating that serum TSH level is reduced in some older subjects, which can be due to changes in the hypothalamus-pituitary-thyroid axis. Other reports have mentioned that this alteration may be due to reduction of T3 in elderly subjects. Although T4 is not altered, reverse-T3 seems to increase in older population with aging, particularly in those suffering from other diseases [20, 21-24].

Interpretation of TSH and T4 levels is difficult in patients, particularly in elderly patients. The prevalence of hypothyroidism is nearly twice among younger women compared to older women. It seems that the incidence of subclinical hypothyroidism is higher than that of overt hypothyroidism, which may be influenced by diet and iodine consumption. Studies on hypothyroidism have suggested thyroid function assessment in elderly men and women, even if these subjects do not have any particular complaints [25-27].

Another study indicated that the incidence of hypothyroidism in older men and women is about 6% and 2.5%, respectively (mean incidence 4-5%). According to recent investigations, serum level of hormones indicates hypothyroidism. In some cases, serum T4 level does not change despite the elevation of serum TSH level. Therefore, TSH seems to be the key hormone for diagnosis of hypothyroidism. When T4 is in the normal range despite the elevated TSH level, some manifestations of hypothyroidism may be still present. This condition is referred to as subclinical hypothyroidism [28-29].

Thyroid dysfunction is common, particularly among women and older subjects. The similarity of hypothyroidism and aging makes the diagnosis difficult for older individuals. The main aim of this study is to review the literature on hypothyroidism in the elderly [30-33].

Thyroid hormones biosynthesis and regulation

The mechanism behind T3/T4 biosynthesis is dependent on the cooperation between three endocrine glands; hypothalamus, pituitary, and thyroid, which are coordinately responsible for the production of the thyroid hormones. In healthy subjects, the thyrotropin-releasing hormone is released from the hypothalamus under the influence of serum T4 level, mainly to later affect T3 levels. Thyroid abnormality occurs when this coordination changes due to any malfunction [34-38].

Hypothyroidism occurs when serum T4 level is lower than the normal range, which could be due to thyroid and metabolic disorders, TSH receptor abnormality and anatomical alterations [8,9]. Hypothyroidism can be divided into three categories including primary, secondary and tertiary. Suppressed serum T3 and T4 levels are the result of all three categories. Although primary hypothyroidism is mainly due to thyroid disorders, the cause of secondary and tertiary types may be the hypothalamic-pituitary axis.

TSH and T4 are the key elements in thyroid function test, although the estimation of autoantibodies against thyroid and TSH receptor may be useful for assessment of thyroid function [2,6,8,23, 39-41].

normal.

Laboratory measurement of thyroid hormones

Thyroid hormones measurement has been possible for decades using radio- and enzyme-immunoassays. Based on these laboratory techniques, thyroid dysfunction can be classified into overt and subclinical, following the measurement of TSH, T3 and T4 levels. Thyroid dysfunction reduces or increases levels of T4 and TSH. These levels are detected in upper and lower laboratory reference values, defining hypothyroidism or hyperthyroidism. Laboratory measurement can help determine the nessecity for continuation of hormone therapy [2,6,17,42-44].

Thyroid function tests

Factors involved in thyroid function assessment include total T3, free T3, total T4 and free T4. Free hormones are the biologically active forms, which constitute for about 1-5% of total thyroid hormones. Other T3 and T4 play the main roles in metabolism of the thyroid hormones. Their measurement is the basis for assessment of thyroid hormones abnormalities [5, 16-19].

Types of thyroid disorders

Hypothyroidism can be divided into two types: overt and subclinical. In overt hypothyroidism, TSH is elevated and T4 is mainly suppressed. While, in the subclinical form, TSH is elevated and T4 is within the normal range. Differentiation of true hypothyroidism from subclinical hypothyroidism is possible via careful laboratory assessments. TSH seems to be the key hormone for the diagnosis of

hypothyroidism. However, T4 measurement should be accompanied with TSH measurement to differentiate overt hypothyroidism from the subclinical form. In addition, T3 or triiodotyronines should be checked for a possible reduction in its concentration [3,6].

Clinical manifestations of overt hypothyroidism

The full-blown expression of hypothyroidism is known as myxedema, which is accompanied with severe adverse effects ranging from gastrointestinal problems to several other disorders. These complications can be prevented on time if the origin of dysfunction could be corrected by thyroxine hormone replacement therapy (HRT) until the serum thyroxin level returns to normal concentration. There is some disagreement on the treatment of subclinical hypothyroid in the elderly. Although correction of subclinical hypothyroidism can be helpful for prevention of complications of hypothyroidism, it cannot be stated confidently that all symptoms of hypothyroidism such as cardiovascular dysfunction and potential fetal complications will be corrected in the older patients. Nevertheless, subclinical hypothyroidism can eventually lead to overt hypothyroidism if not treated. Thyroid dysfunction commonly occurs among elderly, specifically among elderly women. Therefore, it is important to carefully diagnose thyroid disorders and hypothyroidism in these subjects, and distinguish between the physiologic changes of normal aging and symptoms of hypothyroidism [12-15, 21,22].

In the past forty years, measurement of TSH level has been used for evaluation of thyroid function in laboratory procedures. Initially, laboratory techniques were not capable of detecting the exact level of this hormone. Nowadays, medical laboratory techniques and **immunoassay** procedures can measure lowest amounts of TSH in subjects with suspected thyroid disorders [11, 23, and 24]. It is generally believed that elevated TSH and suppressed T4 indicate overt hypothyroidism, which is mainly due to inability of the thyroid gland to produce thyroid hormone. This could be caused by deficiency in enzymes responsible for biosynthesis of thyroid hormones [21, 24-29]. Thyroglobulin is a glycoprotein containing about 5000 amino acids that plays an important role in biosynthesis of thyroid hormones [7].

Studies indicated that factors within the thyroid gland such as TSH receptor antibodies, thyroid enzymes involved in T4/T3 synthesis, and thyroglobulin may interfere with proper pathways, leading to thyroid hormone biosynthesis. Chronological age and race can also play important roles in thyroid hormones metabolism [8, 20, 30]. It seems that levels of thyroid hormones are altered mainly in women. Studies have demonstrated that middle-aged subjects require higher concentration of pituitary TSH to stimulate T3/T4 production by the thyroid gland. It is recommended to investigate thoroughly whether anatomical alterations in the elderly with subsequent change in the TSH receptor (causing low affinity of TSH to its receptor) or T3/T4 synthesis pathways could increase the concentration of TSH required by thyroid [8].

Treatment of subclinical hypothyroidism

Subclinical hypothyroidism can eventually lead to overt hypothyroidism if not treated. Previous studies have shown that (HRT) does not improve the symptoms of subclinical hypothyroidism in older individuals. However, other studies indicated that some of the symptoms related to subclinical hypothyroidism (cardiovascular symptoms, lipid profile and fatigue) could be recovered in the elderly following thyroxine replacement therapy

[3,4,10,11,31-37]. Since this disease can progress into overt hypothyroidism, it is important to measure both TSH and thyroid peroxidase antibodies. It seems that simultaneous increase in both TSH and autoantibodies against the enzyme may indicate subclinical hypothyroidism-originated overt hypothyroidism. Since elderly subjects are more prone to hypothyroidism with eventual adverse outcomes, it is vital for such patients to be monitored carefully to avoid further complications [2, 45-53].

Summary and key points

1. Thyroid hypothyroidism can be divided into two types: overt and subclinical. In overt hypothyroidism, TSH is elevated and T4 is mainly suppressed. In subclinical hypothyroidism, TSH is elevated but T4 is within the normal range.
2. In some clinical settings, subclinical hypothyroidism is mistreated as overt hypothyroidism, since it is believed to be the pre-condition for true hypothyroidism.
3. Hypothyroidism commonly occurs in older subjects, especially in older women.
4. Clinical manifestations of hypothyroidism can be mistaken with physiological changes of normal aging.
5. Reduction in the concentration of T3 in some older subjects has been reported.
6. It seems that T4 is not altered with aging, while reverse-T3 increases in older population with aging, particularly in those with other diseases.
7. It seems that thyroid hormone levels are altered mainly in women. Studies have demonstrated that middle-aged subjects require higher concentration of pituitary TSH to stimulate T3/T4 production by the thyroid gland.
8. Subclinical hypothyroidism can eventually lead to overt hypothyroidism if left untreated.
9. Some studies indicate that older people show no improvement following treatment with HRT.
10. Other studies indicated that some symptoms of subclinical hypothyroidism (cardiovascular symptoms, lipid profile and fatigue) in the elderly could be improved following thyroxine replacement therapy.

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