

## Review Article

# Hypothyroidism in elderly patients

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**Hypothyroidism is more common in the elderly population, partly because of the increased prevalence of autoimmune thyroiditis. Accurate diagnosis of the disorder is complicated due to a multitude of factors. Management in the elderly depends on factors with respect to the metabolism of thyroid hormone and is also affected by drug interactions. Over zealous treatment can lead to fatal arrhythmias and loss of bone density which has to be taken care of while treating the patient. In patients of mild or subclinical hypothyroidism where treatments were aimed at normalizing thyroid functions, the results have been conflicting.**

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**Key words :** Hypothyroidism, India, Elderly, Treatment.

There has been a paradigm shift in the recent decades with respect to the health of elderly population. Hypothyroidism is a disease that increases in both prevalence and incidence among the elderly. The challenge for the clinician being that the clinical manifestations of hypothyroidism may be less obvious in the setting of somatic complaints and establishing a diagnosis is cumbersome due to a relative lack of referable complaints, other confounding findings related to comorbid conditions associated with ageing process, upward rise in TSH levels that may occur with increasing age and changes in thyroid hormone levels that may be related to non-thyroidal illness.

### *Prevalence / Burden :*

Hypothyroidism is commoner in elderly population groups, in comparison to younger individuals, and is higher in the female gender attributable probably to the increasing incidence and prevalence of autoimmune thyroiditis, it has also been seen that the incidence of hypothyroidism increases with increasing age<sup>1,2</sup>. As with other diseases, incidence and prevalence estimations have fluctuated probably because varied population groups were studied, as well as due to variety of criteria used in defining the disorder. In a survey done in the past, which employed the calculated free thyroxine index, it was found that about 2.3% patients had the required criteria to diagnose hypothyroidism<sup>2</sup>. Other community based studies of healthy adult population showed that 7 to 14% of elderly population had serum TSH levels above the normal upper limit of reference values<sup>3,4</sup>. In some studies, prevalence of hypothyroidism in community population and elderly hospitalized group have been found to be comparable. The Third Na-

tional Health and Nutrition Examination Survey (NHANES III) showed that a significantly higher number of women in age group of 50-59 and 60-69 met the benchmark for diagnosis of hypothyroidism (clinical and subclinical) in comparison to men who were in similar age brackets. A study assessing elderly (geriatric) patients on medical treatment reported that about 17% of males and 15% of females had not been diagnosed with hypothyroidism previously<sup>5</sup>. A study of older adults reported that every one out of 10 women and one out of 50 men were on thyroid hormone supplementation which had been on prescription<sup>6</sup>, and within this population, about 12% of the women and 29% of the men were found taking thyroid hormone for reasons deemed inappropriate. It is quite certain that the estimations of the prevalence and incidence of hypothyroidism in the elderly population need to consider the ever-increasing evidence that normal TSH values and curves of distribution seem to take a shift to the higher side with increasing ages. Study of TSH levels with respect to age and anti-thyroid antibody titers measured as part of the recent NHANES study reported that 12% of subjects over 80 years without evidence of underlying autoimmune thyroiditis had TSH levels higher than 4.5 mIU/L<sup>7</sup>. With respect to the role of dietary iodine, most studies have inclined towards the notion that iodine deficiency appears to have a protective role against the development of hypothyroidism in the elderly<sup>8,9</sup>. A study done recently in North India showed that a significantly higher proportion of women *versus* men (15.86% *versus* 5.02%) and elderly *vs.* younger (13.11% *versus* 7.53%) adults were diagnosed with hypothyroidism. Thus, females and elderly were found to be having a significant link with developing hypothyroidism, autoimmune mechanisms probably appeared to play a causative role in a large proportion of patients<sup>10</sup>. A recent study in South India showed that thyroid function disorders are common in elderly; affecting about 14% of study population, overt hypothyroidism being the most

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common thyroid disorder (5.81%), followed by subclinical hypothyroidism (5.54%). Abnormalities in thyroid function were shown to have an increasing incidence with age in both genders<sup>11</sup>.

### *Physiology and Thyroid Function Tests :*

There are various implications of understanding the physiological changes in levels of TSH with increasing age. Regarding physiology, the aging thyroid gland is characterized by several microscopic changes.

**Microscopic Changes :** Prominent changes include arise in the inter-follicular connective tissue. The size of the follicles decreases and so does the colloid content (the matrix in which the hormone is stored). With increasing age, these areas begin to lack colloid content, while in other areas the follicles are composed of pale colloid, that indicate a decreased store of thyroid. The epithelium of the glands undergo atrophy with flattening and reduction in size of the lining cells. The bulk weight of the gland itself decreases, with a slight increase in volume. Basal utilization of oxygen per unit surface area reduces which is similar to that in patients with hypothyroidism. Therefore, it can be said that the researchers who postulated that hypothyroidism is probably a normal result of the aging process were correct in their own way, and some even suggested that following the administration of thyroid hormone to older patients, their BMR (basal metabolic rate) showed a rise.

There have been many studies that have investigated the role of thyroid gland and its function in aging. Recent studies also show a rise in serum TSH levels with age, independent of the presence of antithyroid antibody<sup>6</sup>. While contrasting studies have demonstrated a decrease in serum TSH in older population<sup>2,13</sup>, the relationship between TSH values and age seems to depend on the nature of thyroid pathology. In patients with Hashimoto's thyroiditis, there is a tendency of TSH to increase with rising age<sup>14,15</sup>, whereas in populations with iodine deficiency where the thyroid pathology includes nodularity and increase in thyroid autonomy with age, a fall in TSH levels are suggested with increasing age<sup>16</sup>. With regards to free T3 levels, most studies have demonstrated an age-dependent decline, while free T4 levels remain quiteunaltered<sup>12,13</sup> while rT3 levels show a rise with increasing age. It is interesting to note however that interpreting thyroid functions in elderly is complex due to the presence of chronic illnesses and consumption of multiple drugs by the patient<sup>17</sup>. There is now evidence that raised TSH levels are associated with longer life, a study reported that serum TSH levels were significantly higher in centenarians (mean age=98 years) as compared to controls<sup>18</sup>. Most other studies have also depicted higher TSH levels (mean age=85 years) and low to low-normal FT4 levels (mean age=78 years) to have an association with a longer period of survival in elderly<sup>19,20</sup>. The

hypothesis to the association of a higher TSH level with longevity may be attributable to a reduced bioactivity of thyroid hormone, which causes a lower basal metabolic rate and potentially serves to be an adaptation to prevent catabolism in the elderly<sup>20</sup>.

### *Etiology In Elderly :*

Autoimmune thyroiditis is the commonest cause of hypothyroidism among the elderly, as it is in the younger population<sup>21</sup>, this was established in a study of patients attending an endocrinology clinic where 57% of patients above the age of 55 years were diagnosed as having autoimmune thyroiditis while 32% carried a diagnosis of postsurgical hypothyroidism and 12% had a diagnosis of post-radioiodine hypothyroidism<sup>21</sup>. Only about 2% of patients in this population presented with evidence of secondary hypothyroidism.

### *Clinical Features :*

**Classical Symptoms :** Easy fatiguability, generalized weakness, weight gain, anorexia, dry skin, pedal edema, goitre, constipation, sleep apnoea, cold intolerance, hairloss, confusion, lassitude, depression.

**Classical Signs :** Facial puffiness, dry skin, bradycardia, myopathy, recession of eyebrows and frontal hair, cerebellar signs, effusions, delayed ankle jerk relaxation.

#### **Two signs found in more than 50% elderly patients<sup>22</sup>:**

- Fatigue.
- Weakness.

#### **Four signs found less frequently in elderly compared to young :**

- Chilliness, Parasthesias, Weight gain, Cramps.

#### **Clinical presentation that heighten suspicion in older age group compared to young —**

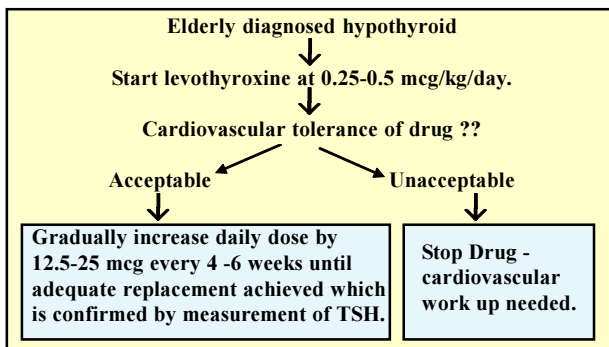
- Congestive cardiac failure (restrictive cardiomyopathy)
- Fecal impaction (due to retarded stool movement through bowel)
- Macrocytic anemia
- Unexplained elevations in plasma cholesterol or triglyceride levels
- Vague arthritic complaints
- Psychiatric complaints- depression, myxedema madness. Rare- syncope, seizures .
- Physical findings evident in hypothyroid elderly individuals may include bradycardia, diastolic hypertension, pallor, dry skin, coarse hair, hoarseness, dysarthria, delayed relaxation of deep tendon reflexes, and mental status changes.
- Other features suggestive- Thyroidectomy scar, impaired cerebellar function, history of radioiodine therapy, goitre, family history of thyroid disease.

### *Morbidity :*

Medical complications of hypothyroidism which are

severe are also more common in the elderly, as evidenced by the fact that almost all patients presenting with myxedema coma are elderly, and those patients in this age group may be at a higher risk for developing complications related to surgery (perioperative and intraoperative). A comparative study of patients with unrecognized hypothyroidism with controls matched for age, sex, and operative procedure showed an increased rate of heart failure, intraoperative hypotension and postoperative gastrointestinal and neuropsychiatric complications in hypothyroid patients<sup>23</sup>.

### *Treatment :*



A recent survey of the members of the American Thyroid Association confirmed that this general strategy was adopted in practice<sup>24</sup>. A trial showed that elderly patients devoid of underlying cardiac illnesses could be started safely on full replacement doses of thyroxine (1.6mcg/kg) without side effects<sup>25</sup>. Following a change in dosage of thyroid hormone, TSH levels should be measured every four to six weeks and most experts recommend a target level of normal TSH range in the elderly<sup>26</sup>. Whereas an estimated 39% of ATA members suggest targeting a TSH range of 0.5-2.0 mIU/L while treating younger population with hypothyroidism, a comparable number suggested that they were generally more liberal with regards to their approach to older patients, targeting TSH ranges of 1.0-4.0 mIU/L. While an optimal target would be to supplement thyroid hormone to a level which corrects the deficiency completely, patients with coronary heart disease may be unable to tolerate those doses of thyroxine. One study of patients with known coronary artery disease and primary hypothyroidism reported that precipitation of angina symptoms limited titration of thyroxine in two-thirds of cases, while precipitation of hypothyroid symptoms limited titration of anti-anginal agents in one-third of cases, and despite adding propranolol at maximally tolerated doses, about 46% of the patients suggested that the control of their angina and hypothyroid symptoms was only fair to poor<sup>27</sup>. A study proposed that lean body mass was probably a better predictor of replacement doses each day rather than age or weight<sup>28</sup>, while another study reported that

majority of the age-dependent differences in thyroxine requirements noted might be due to the effects of chronic illnesses, because a significantly lower mean daily replacement dosing was seen in older patients being treated for other chronic medical disorders<sup>29</sup>. A study tracking the variations in thyroxine requirements of older patients over time based upon the cause of their primary hypothyroidism showed that daily replacement doses increased in patients who initially presented with autoimmune thyroiditis or postsurgical hypothyroidism, reduced in patients who initially presented with post-ablative hypothyroidism, and was unchanged in patients who initially presented with subclinical hypothyroidism or drug-induced hypothyroidism<sup>30</sup>. In situations where cognitive or functional impairment may make it difficult for patients to comply with daily administration of thyroxine, alternative dosing schedules may be considered. Polypharmacy is a major issue with many drugs known to interfere in metabolism of thyroxine like calcium carbonate, ferrous sulfate, sucralose, aluminum hydroxide, cholestyramine, colestipol, raloxifene and estrogen replacement therapy. Long-term administration of phenytoin, carbamazepine, phenobarbital, or rifampin in the setting of treated primary hypothyroidism typically increases metabolism of thyroxine and increase in the dose of thyroxine required to provide optimal replacement. Overtreatment with excessive doses of thyroxine may be associated with significant morbidity in the elderly. Palpitations, anxiety, tremulousness, irritability, insomnia, heat intolerance, hyperdefecation, and weight loss may be precipitated or exacerbated by iatrogenic thyrotoxicosis. A study that tracked bone mineral density changes in women treated with thyroxine documented greater mean rates of bone mineral loss in the lumbar spine of women with suppressed TSH levels<sup>31</sup>. With respect to mild/subclinical hypothyroidism, the consensus recommendations of the American Thyroid Association and the American Association of Clinical Endocrinologists advise treatment of subclinical hypothyroidism involving a TSH level greater than 10.0 mIU/L. In patients with lesser elevations of TSH, however, clinical judgment is critical in deciding whether to treat or monitor<sup>32</sup>. Consequently, a recent consensus statement issued by an expert panel recommended that cases of mild hypothyroidism presenting with TSH levels ranging from 4.5-10.0 mIU/L be treated on a provisional basis, with continuation of therapy predicated on clear evidence of improvement in symptoms consistent with thyroid hormone deficiency<sup>33</sup>.

### *Conclusion :*

Hypothyroidism in the elderly population is a common condition which requires a keen clinical suspicion for diagnosis due to obscuration of many signs and symptoms compared to the younger population. The management of

hypothyroidism in elderly is challenging due to physiological changes with age, cardiac, bone problems and differences in treatment responses to levothyroxine. Therefore a clinician needs to be alert and aware of the issues related to hypothyroidism in elderly.

**Conflict of interests : None**

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