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Risk of Progression to Overt Hypothyroidism in Geriatric Patients with Subclinical Hypothyroidism

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A B S T R A C T

Aim: The purpose of this research is to assess the natural course of SCH and find risk variables possibly causing overt hypothyroidism (OH) in elderly people.
Method: Over a one-year period, this prospective observational research tracked 58 individuals with SCH under evaluations every six months to track the progression of the disorder.
Results: Out of the total number of patients (16%), 8 experienced progressions to overt hypothyroidism that is, a thyroid-stimulating hormone (TSH) level of 10 IU/L or above during the one-year follow-up study. Out of all the patients, 34 people 68% of the sample were categorized as remaining members of the SCH group. Of the fifty people, eight had TSH normalized; this is sixteen percent of the total. In the group tested positive for anti-thyroid peroxidase antibodies (anti-TPO), the rate of progression to overt hypothyroidism (OH) was 33.33%; in the group tested negative for anti-TPO, this rate was 8.57%. The group who tested positive for anti-TPO antibodies progressed much more quickly than the group that tested negative ($p<0.023$). Sex, glycemic status, central adiposity, and baseline TSH>6 had no correlation found with development to OH.
Conclusion: regardless of whether a person has a real thyroid disease or not, it has been shown that TSH levels in blood tend to grow as one ages. In India's geriatric population with subclinical hypothyroidism (SCH), the incidence of progression to osteoporotic hip (OH) is very high-18.97%. The existence of anti-TPO antibody was the sole element that fairly projected the incidence of OH.

Keywords: *Hypothyroidism, geriatric patients.*

INTRODUCTION

The most often occurring thyroid condition is subclinical hypothyroidism (SCH), which is biochemically defined by a continuous increase in serum thyroid-stimulating hormone (TSH) levels for 12 weeks or more

while serum free thyroxine (FT4) levels stay within the normal range. Two more categories may be distinguished among patients with SCH: those with somewhat raised TSH levels (4.5–10 mIU/L) and those with much raised TSH levels (>10 mIU/L [1, 2]. Although it is more common in elderly populations [3-5], general population ranges from 4-10% have SCH prevalence.

Recognised as an early phase of thyroid illness, subclinical hypothyroidism (SCH) may develop to overt hypothyroidism (OH). Studies reveal that the pace of development to OH varies; estimates range from 3% to 18% annually [6–10]. Under a 10-year span, Huber et al. studied 154 female patients with SCH and found that 57% of participants remained to show moderate thyroid failure, 34% proceeded to OH, and 9% restored to normal TSH levels [10]. With an odds ratio of 14 (95% CI, 9-24) compared to TSH levels below 6 IU/L [11], the Wickham research also indicated that a TSH level more than 6 IU/L is a significant predictor of progression to OH.

Still, circulating TSH has been shown to rise with age, independent of any real thyroid dysfunction. Therefore, when facing a rise in circulating TSH levels in the elderly, particularly in the oldest old, it is crucial to have a suitable diagnostic approach, complete of clinical picture as well as laboratory and imaging procedures.

In this scenario, early identification of individuals at risk of developing overt hypothyroidism (OH) or returning to normal is very essential. The main goal of this research was to find the rate of development to OH for patients with subclinical hypothyroidism (SCH). Finding the risk variables connected to progression to OH would help to guide follow-up plans and improve patient treatment in general.

METHODOLOGY

This research is a prospective observational study that was done between the years 2021 and 2023. The research involved individuals who met the following inclusion criteria: age more than 18 years, recent diagnosis of spontaneous SCH (with normal total T4 and TSH levels between 4.2 IU/L and 10 IU/L). This research excluded pregnant women, individuals undergoing radio-iodine treatment, and patients with a past history of thyroxine therapy. There were no patients taking any medication that affects the levels of thyroid hormones. The diagnosis of subclinical hypothyroidism (SCH) was made based on an elevated thyroid-stimulating hormone (TSH) level, ranging from more than 4.2 IU/L to less than 10 IU/L, along with normal levels of total triiodothyronine (TT3) and total thyroxine (TT4). A total of 50 individuals with SCH were included in the current investigation. Patients' data on age, sex, body mass index (BMI), waist circumference (WC), blood glucose (BG), and anti-TPO antibody were obtained on each visit using a standardized manner. The weight was determined using a weighing equipment that has a precision of 0.1 kg. The height was determined using a stadiometer with a precision of 0.1 cm. The BMI was determined by dividing the weight (in kilograms) by the square of the height (in meters).

Two visits were scheduled with a six-month gap for a duration of one year. A follow-up thyroid test was conducted after one month to exclude the possibility of natural fluctuations. During each appointment, the thyroid profile was examined and demographic information was noted. During the subsequent examination, we classified patients with OH as those with a TSH level of 10 IU/L or above.

The recorded data was summarized using SPSS version 22. A p-value less than 0.05 was deemed statistically significant.

RESULTS

This research recruited a total of 50 patients. Out of the total, there were 16 males and 34 females. The baseline characteristics of all patients were presented in Table 1. The mean ± standard deviation (SD) values for age, body mass index (BMI), and waist circumference (WC) were 65.34±16.82 years, 28.35±7.34 kg/m2, and 92.35±24.35 cm, respectively. There were no notable differences in age, BMI, and WC between the male and female groups. Central obesity was seen in 84% of the total population, 81.25% of males, and 82.86% of females. There was no statistically significant difference in the prevalence of central obesity in men and females.

The prevalence of diabetes mellitus (DM) was 32% overall, 56.25% among men, and 20.59% among females. The prevalence of Anti-TPO antibody was 30% in the whole population, 12.5% in men, and 38.23% in females. The prevalence of diabetes mellitus (DM) was substantially higher in men than in females. The incidence of autoimmunity was comparable in both groups. The mean ± standard deviation (SD) values of total T3, total T4, and TSH at baseline were 114.75±26.7 ng/dl, 7.67±1.76 micro gm/dl, and 6.75±1.64 IU/L, respectively. There were no statistically significant differences in TT3, TT4, and TSH levels between the male and female groups.

Table 1: Baseline Demographic Profile of Study Population.

Parameters		**All, N (%)**	**Male, N (%)**	**Female, N (%)**	**P value**
Number		50	16 (32)	34 (68)	
Age (years)		65.34±16.82	67.35±16.35	62.35±18.46	<0.057
BMI (kg/m^2)		28.35±7.34	24.34±5.35	28.46±4.46	<0.08
WC		92.35±24.35	90.36±7.36	93.34±11.24	<0.27
Central obesity	Present	42 (84)	13 (81.25)	29 (82.86)	<0.96
	Absent	8 (16)	3 (18.75)	5 (17.14)	
DM	Present	16 (32)	9 (56.25)	7 (20.59)	<0.01
	Absent	34 (68)	7 (43.75)	27 (79.41)	
Anti TPO	Present	15 (30)	2 (12.5)	13 (38.23)	<0.13
	Absent	35 (70)	14 (87.5)	21 (61.77)	
Total t3		114.75±26.7	116.76±24.85	115.36±24.25	<0.78
Total T4		7.67±1.76	7.57±1.47	8.01±1.54	<0.23
TSH		6.75±1.64	6.38±1.47	6.57±1.87	<0.54

At one-year follow up examination 8 (16%) patients progressed to OH (defined as TSH ≥10 IU/L). The 34 (68%) patients remained in SCH category. In 8 (16%) patients TSH normalized. In anti-TPO positive group rate of progression to OH was 33.33% while in negative group it was 8.57%. Rate of progression was significantly higher in anti-TPO positive group as compared to negative (p<0.023). Sex, glycemic status, central obesity and baseline TSH>6 was not associated with progression to OH (Table 2).

Table 2: Predictors of Progression in Study Population.

Pararmeters		**Progressor, N (%)**	**Non-progressor, N (%)**	**P-value**
Sex	Male	3 (17.65)	14 (82.35)	<0.77
	Female	5 (17.65)	28 (82.35)	
Glycemic status	DM (Present)	2 (12.5)	14 (87.5)	<0.306
	DM (Absent)	6 (17.65)	28 (82.35)	
Anti TPO	Present	5 (33.3)	10 (66.7)	<0.02
	Absent	3 (8.57)	32 (91.43)	
Central obesity	Present	6 (14.29)	38 (85.71)	<0.789
	Absent	2 (25.0)	6 (75.0)	
TSH	<6	5 (22.73)	17 (77.27)	<0.394
	>6	3 (10.71)	25 (89.29)	

DISCUSSION

As individuals age, their ability to absorb and use iodine decreases, resulting in changes to the thyroid's response to TSH (thyroid-stimulating hormone). Furthermore, alterations have been documented in the TSH bioactivity,

the sensitivity of thyrocytes to TSH, thyroid hormone metabolism, and the receptors and co-factors that regulate the response to T3 input [12]. Collectively, these activities lead to a decrease in the synthesis of thyroid hormones [13-15]. Individuals over the age of 80-85 years showed a nocturnal increase in TSH, which was partly or entirely lost due to a weakened inhibitory action of corticosteroids. This suggests that there is an age-related degradation of the hypothalamus. Several observational studies have reported a more intricate association between TSH levels and the aging process, even when excluding people with thyroid illness or autoimmune. Indeed, certain studies (typically case-control) have indicated a tendency towards decreased levels of TSH in individuals over the age of 75-80 and centenarians [18]. However, more recent cohort studies have shown a contrasting pattern in TSH levels as people age, with a shift towards higher values in older individuals. Specifically, for those aged 80 years and older, the highest value within the 95% confidence range is around 6.0 mIU/L, and it increases to 8.0 mIU/L for those over 90 years old [19-21]. Some writers have interpreted the decreased levels of TSH in centenarians as a resetting of thyroid function in the brain, which helps to avoid excessive breakdown of tissues and supports the process of "physiological aging" [22]. In order to address the lack of comprehensive data on the natural progression of SCH in India, we conducted a prospective real-world research with a cohort of 50 patients. We also examined potential prognostic markers associated with the development of orthostatic hypotension (OH). To the best of our knowledge, this research is the first from India to evaluate the natural progression of subclinical hypothyroidism in elderly people. In the current investigation, the rate of advancement was considerably greater in the group that tested positive for anti-TPO antibodies compared to the group that tested negative ($p<0.023$). There was no association seen between sex, glycemic status, central adiposity, baseline TSH>6, and progression to OH. In a research conducted by Huber et al [23], it was shown that 28% of the participants experienced orthostatic hypotension (OH) over time. The majority, 68%, remained in a condition of subclinical hypothyroidism (SCH), while a small percentage (4%) returned to a normal state. The variations in the data may be attributed to factors such as variations in patient age, differences in research methods, and variations in the study population. The average age of patients in our research was much greater than that of the Huber et al. study. It is a well-established fact that as individuals age, the average level of TSH (thyroid-stimulating hormone) in their bodies tends to rise. Consequently, this may lead to the misclassification of many euthyroid people as having subclinical hypothyroidism (SCH). As they can maintain normal thyroid function, they will not develop overt hypothyroidism. The rate of advancement will be lower in the older population cohort compared to the lower age cohort. Another possible explanation for the increased prevalence of optic hypoplasia in Indian patients with septo-optic dysplasia might be attributed to the relatively lower size and weight of their thyroid gland compared to Caucasians [24]. Reduced size and weight result in a decreased thyroid hormone reserve, leading to a faster development to OH.

CONCLUSION

Hypothyroidism, whether it is overt or subclinical, is a common chronic condition that affects older individuals. However, it has been shown that levels of TSH (thyroid-stimulating hormone) grow with age, regardless of whether there is an actual thyroid illness present. The rate of progression to osteoporotic hip (OH) is very high (18.97%) in elderly people with subclinical hypothyroidism (SCH) in India. OH was only predicted by the presence of anti-TPO antibody.

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