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Original Research Article

Assessing Progression to Overt Hypothyroidism in Patients with Subclinical Hypothyroidism: A Retrospective Study

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Abstract

Aim: The aim of the study was to determine the spontaneous course of SCH and to identify the risk factors, which enhances the occurrence of overt hypothyroidism (OH).

Methods: This was a retrospective study conducted in the Department of Medicine, Katihar Medical College and Hospital, Katihar, Bihar India for 18 months. A total of 50 patients were recruited in this study.

Results: The mean ± SD age, BMI, and WC were 42.28±12.48 years, 26.49±4.82 kg/m2, and 94.12±19.81 CM. No significant age, BMI, or WC difference existed between men and women. Central obesity affected 84%, 80%, and 85.71% of men and females, respectively, with no significant difference. Diabetes was prevalent in 30%, 53.34%, and 20% of men and females. Males and females had 34%, 20%, and 42.85% anti-TPO antibodies. Eleven (18.97%) individuals advanced to OH (defined as TSH ≥10 IU/L) at one-year follow-up. The advancement rate was considerably greater in the anti-TPO positive group compared to the negative group ($p<0.023$).

Conclusion: The first risk stratification may identify SCH patients at highest risk for OH, which requires therapy.

Keywords: SCH, OH, Progression, Anti-TPO antibody

Introduction

Thyroid problems are the most common endocrine disorders worldwide. Reports indicate that almost 42 million people in India suffer from thyroid problems. [1] Iodine deficiency is the main worldwide factor leading to hypothyroidism. [2] Subclinical hypothyroidism (SCH) is a common endocrine disorder that is widespread in both India and worldwide. [3] Subclinical hypothyroidism is defined by elevated amounts of thyrotropin (TSH) in the bloodstream, together with normal levels of total thyroxine or free thyroxine (T4), and the lack of any symptoms associated with hypothyroidism. SCH is often detected incidentally, since patients usually exhibit little or no signs of thyroid disorder. There is a lack of study evaluating the natural course of subclinical hypothyroidism (SCH) in India. [4] persons with subclinical hypothyroidism (SCH) often do not exhibit any symptoms, however around one-third of persons may develop signs that suggest a deficiency in thyroid hormone. Common signs of this condition may manifest as parched skin, fatigue, cognitive decline, muscle spasms, swollen eyes, heightened sensitivity to low temperatures, and a raspy voice. [5] This syndrome mostly occurs in persons with early-stage Hashimoto's disease and is common, affecting around 7 to 10% of older women. [6,7]

Subclinical hypothyroidism may arise from either internal reasons, such as chronic autoimmune thyroiditis, subacute thyroiditis, or postpartum thyroiditis, or external ones, such as thyroidectomy, 131I treatment, antithyroid drugs, or inadequate thyroid hormone replacement therapy. SCH is often associated with dyslipidemia, abortion, miscarriage, endothelial dysfunction, coronary artery disease, peripheral vascular disease, aortic atherosclerosis, myocardial infarction, and other ailments. [8-10] SCH, or subclinical hypothyroidism, refers to an initial phase of thyroid dysfunction that often progresses to overt hypothyroidism (OH). The prevalence of development into overt hypothyroidism ranges from 7.8% to 17.8% in various studies. [11] Wickham's research revealed that those with a TSH level over 6 IU/L had a high likelihood of developing OH. The odds ratio for this progression was 14, with a 95% confidence range ranging from 9 to 24, as compared to people with a TSH level < 6 IU/L. [12] Other factors that may suggest the probability of progression include the presence of antithyroid antibodies, being female,

having a moderately low level of FT4, receiving lithium medication, undergoing radioiodine ablation for Graves' disease in the past, and having a history of external radiation therapy for non-thyroid malignancies. Due to the high prevalence of this disorder and the challenges it presents, it is essential to determine the inherent course of the disease. It is vital to identify individuals who may either acquire orthostatic hypotension or experience improvement in this condition.

The research aimed to determine the natural course of subclinical hypothyroidism (SCH) and identify the variables that contribute to the development of overt hypothyroidism (OH).

Materials and Methods

This was a retrospective study conducted in the Department of Medicine, Katihar Medical College and Hospital, Katihar, Bihar India for18 months. A total of 50 patients were recruited in this study.

Inclusion & Exclusion Criteria

The research included patients who were over 18 years old and had recently been diagnosed with spontaneous SCH (subclinical hypothyroidism), characterized by normal total T4 levels 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.

Methodology

There were no individuals who were taking any medication that might affect their thyroid hormone levels. The diagnosis of subclinical hypothyroidism (SCH) was made based on an elevated thyroid-stimulating hormone (TSH) level, which was more than 4.2 IU/L but less than 10 IU/L, along with normal levels of total triiodothyronine (TT3) and total thyroxine (TT4). The current research included a total of 58 participants with SCH. Patients' age, sex, body mass index (BMI), waist circumference (WC), blood glucose (BG), and anti-TPO antibody data were gathered on each visit using a preset format. The weight was determined using a weighing equipment that has a precision of 0.1 kg. The stadiometer used for measuring height has a precision of 0.1 cm. The BMI was computed by dividing the weight (in kilograms) by the square of the height (in meters). Two visits were scheduled with a six-month gap during the course of one year. The thyroid test was repeated after one month to exclude the possibility of natural fluctuations. At each appointment, the thyroid profile was checked and demographic information was collected. During the subsequent examination, we classified patients with OH as those with a TSH level of 10 IU/L or above.

Analysis

The recorded data were summarized using descriptive analysis. The statistical measures of mean and standard deviation were used to characterize continuous variables. Categorical variables were described using frequency and percentage. The statistical analysis was conducted using SPSS version 26.

Results

Table 1: Baseline demographic profile of study population

Parameters	All, N (%)	Male, N (%)	Female, N (%)	P value
N	50	18	32	
Age (years)	42.33±12.79	46.84±12.02	40.13±12.79	<0.055
BMI (kg/m2)	26.49±4.82	25.12±3.44	27.15±5.28	<0.09
WC	94.12±10.81	95.89±5.71	93.25±12.55	<0.24
Central Obesity				
Present	44 (88)	15 (83.34)	28 (87.50)	<0.94
Absent	6 (12)	3 (16.66)	4 (12.50)	
Diabetes Mellitus				
Present	15 (30)	8 (53.34)	7 (20)	<0.01
Absent	35 (70)	7 (46.66)	28 (80)	
Anti TPO				
Present	17 (34)	3 (20)	15 (42.85)	<0.13
Absent	33 (66)	12 (80)	20 (57.15)	
Total T3	115.66±24.09	116.89±24.08	115.05±24.39	<0.78
Total T4	7.83±1.41	7.53±1.21	7.97±1.49	<0.23
TSH	6.61±1.64	6.79±1.56	6.52±1.69	<0.54

The incidence of autoimmunity was comparable in both groups. The mean ± standard deviation (SD) values of total T3, total T4, and TSH at the beginning of the study were 115.66±24.09 ng/dl, 7.83±1.41 micro gm/dl, and 6.61±1.64 IU/L, respectively. There were no notable disparities in TT3, TT4, and TSH levels between the male and female groups.

Table 2: Predictors of progression in study population

Parameters	Progressor n (%)	Non-progressor n (%)	Odds ratio (95% CI)	P value
Sex				
Male	3 (16.66)	15 (83.34)	1.24 (0.308, 4.8)	<0.74
Female	4 (2.50)	28 (87.50)		
Glycemic status				
Present	3 (16.66)	15 (83.34)	0.45 (0.08, 2.2)	<0.310
Absent	6 (18.75)	26 (81.25)		
Anti-TPO				
Present	5 (29.42)	12 (70.58)	4.60 (1.14, 18.28)	<0.02
Absent	5 (16.16)	28 (84.84)		
Central Obesity				
Present	8 (19.05)	34 (80.95)	0.775 (0.139, 4.44)	<0.770
Absent	2 (25)	6 (75)		
TSH				
<6	5 (25)	15 (75)	1.720 (0.47, 6.63)	<0.356
>6	5 (16.66)	25 (83.34)		

Eleven (18.97%) individuals advanced to OH (defined as TSH ≥10 IU/L) at one-year follow-up. The anti-TPO positive group had 29.42% OH advancement whereas the negative group had 16.16%. The advancement rate was considerably greater in the anti-TPO positive group compared to the negative group ($p<0.023$). Anti-TPO positive patients had a 4.58 (95% CI; 1.14, 18.28) odds ratio for OH progression. Sex, glycemic status, central adiposity, and baseline TSH>6 did not predict OH development.

Discussion

The main factor leading to hypothyroidism during pregnancy on a global scale is iodine deficiency, but in areas with sufficient iodine levels, the most common cause is autoimmune thyroiditis. Other common reasons include the use of radio-iodine therapy, thyroidectomy (surgical removal of the thyroid gland), congenital hypothyroidism (a disease present from birth), drug usage (such as rifampicin and phenytoin), and any disorder affecting the hypothalamic-pituitary system. [13,14] Women with lower thyroid reserves before to pregnancy may have difficulty in meeting the heightened metabolic requirements during pregnancy, potentially leading to the development of hypothyroidism. The maternal levels of thyroid hormone play a vital role in the fetal development, especially in the first trimester when the fetus is incapable of producing iodothyronines until ten weeks of gestation. This is the stage in which the development of the nervous system in the fetus may be impaired due to a deficiency of iodothyronines. [15]

Our research discovered that the existence of thyroid antibody (Anti-TPO) served as a dependable signal of an increased likelihood of developing OH. The odds ratio for developing orthostatic hypotension (OH) in individuals who tested positive for anti-thyroid peroxidase (anti-TPO) antibodies was 4.60, with a 95% confidence range ranging from 1.14 to 18.28. There was no evidence to suggest that sex, glycemic status, central adiposity, and baseline TSH levels over 6 were predictive of developing OH. In our investigation, the rate of progression to orthostatic hypotension (OH) was higher than that seen in the experiment done by Huber et al.[16] Over the course of their decade-long study, 28% of the patients developed OH, while 68% continued to have SCH. A minuscule proportion (4%) shifted into a condition of normalcy. The discrepancies in outcomes might be ascribed to variables such as changes in patient age, disparities in research methodologies, and divergences in the study population. The mean age of the patients in our investigation was comparatively lower in comparison to the study done by Huber et al. [16] As humans age, the average amount of thyroid-stimulating hormone (TSH) tends to increase, which is a well accepted fact. As a result, this might result in the incorrect categorization of several individuals with normal thyroid function as having subclinical hypothyroidism (SCH). Consequently, the pace of progress will be more gradual in the senior population group in comparison to the younger age group. One potential reason for the higher occurrence of optic hypoplasia (OH) in Indian people with septo optic dysplasia (SCH) might be linked to the comparatively smaller size and weight of their thyroid glands in comparison to Caucasians. [17] Diminished size and weight cause a diminished supply of thyroid hormone, resulting in an accelerated progression to OH.

In this investigation, the prevalence of positive anti-TPO (autoimmunity) was found to be 34%, which is much lower than the 76% reported in the Spanish study. [18] This suggests that factors other than autoimmune conditions may be responsible for mild thyroid malfunction in India. The presence of iodine deficiency, endocrine disruptors, and other

goitrogens may lead to a milder type of thyroid dysfunction in Indian patients as compared to persons from Western nations. Kasigi et al. reported a rather low positivity rate (20.5%) for Anti-TPO antibody. [19] Study done by Huber et al [16] shown that patients with a baseline TSH level over 6 had a higher likelihood of developing overt hypothyroidism. Furthermore, Imaizumi et al [20] found that those with a baseline TSH level above 8 were at a higher risk of developing overt hypothyroidism. There was no evidence of any such association. The disparity might be ascribed to the elderly age of the SCH group in their study. Patients whose thyroid-stimulating hormone (TSH) level is less than 6 may be erroneously classified as having subclinical hypothyroidism (SCH) in their studies. Our analysis revealed that the incidence of progression to orthostatic hypotension (OH) in people with diabetes was 11.11%, which was quantitatively lower than the rate of 22.5% seen in those without diabetes. Nevertheless, this discrepancy did not demonstrate any statistical significance. The limited occurrence of progress may be ascribed to the use of metformin in persons with diabetes. Tudor et al also observed a small rate of progress in patients with diabetes. [21]

Conclusion

The presence of anti-TPO antibody in 50 individuals followed for a year indicated OH. Initial risk stratification may identify subclinical hypothyroidism (SCH) patients at greatest risk of orthostatic hypotension (OH) and requiring treatment. Hypothyroidism in pregnant women varies by state in India, however data is scarce. The suggested guidelines for treating subclinical hypothyroidism in pregnant women are also disputed. Thus, further research is needed to overcome diagnostic and therapy shortcomings.

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