Original Research Paper

Volume - 13 | Issue - 04 | April - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Medicine

A STUDY ON SUBCLINICAL HYPOTHYROIDISM IN FEMALES OVER FIFTY YEARS OF AGE

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KEYWORDS :

INTRODUCTION

Subclinical hypothyroidism is defined as patient with normal free T4 but elevated serum TSH level.(1) Various studies have reported the incidence of subclinical hypothyroidism to be 3-15% depending on the population studied.(2,3). Statistical research shows a higher incidence of subclinical hypothyroidism in women and elderly individuals The prevalence of this disorder has increased due to the increased availability of thyroid function testing.

The TSH elevation in such patients is modest, with values typically between 4.5 and 10 mU/L, although patients with a TSH above 10 mU/L more often have a reduced free T4 and may have some hypothyroid symptoms.

Subclinical hypothyroidism may have endogenous causes (chronic autoimmune thyroiditis, subacute thyroiditis, postpartum thyroiditis) or exogenous causes(4) (thyroidectomy, 131I therapy, antithyroid drugs, inadequate thyroid hormone replacement therapy). In the classical population-based study among adults in the English county of Whickham(5) the prevalence was 75 per 1000 women and 28 per 1000 men1. Subclinical hypothyroidism correlates with an increased risk of fatal and non-fatal coronary artery disease (CAD) events and congestive heart failure.(6,7)

The natural history of subclinical hypothyroidism is reasonably well known. Spontaneous return of increased TSH values into the normal range occurs in 5.5% after 1. year.(8) Progression to overt hypothyroidism ranges from 7.8% to 17.8% in various studies(8,9,10).Another report indicates that approximately 30% of patients with subclinical hypothyroidism had developed overt hypothyroidism after 10 years; the higher the initial TSH, the greater the risk(11).

Clinical manifestation of subclinical hypothyroidism include abnormal lipid metabolism) (12,13,14), cardiac dysfunction(15,16) and neurologic and mental dysfunction(17) and several cross-sectional studies have suggested that it confers an elevated risk for atherosclerosis and coronary heart disease.(18,19). The relationship between subclinical hypothyroidism and cardiovascular disease is therefore controversial and possible outcomes of the conditions remain unclear.

Importantly several previous studies suggesting that thyroid autoimmunity is a risk factor for coronary heart disease(20,21) remain surrounded by controversies. Women with subclinical hypothyroidism didn't differ from controls with regard to BMI, Hypertension and Diabetes Mellitus in previous studies(22,23).

This study has been performed to estimate the prevalence of subclinical hypothyroidism and its relation to Hypertension, Diabetes and Ischemic heart disease among women above the age of 50 years attending medical out patient of Raja Rajeshwari medical college and hospital.

MATERIALS AND METHODS

Case selection and Inclusion Criteria

Women above the age of 50 years attending Medical out patient of Raja Rajeshwari Medical college and hospital, Bangalore. A sample of 100 women was randomly selected. Informed consent was obtained from all participants. All the participants were examined for thyroid function. Women with subclinical hypothyroidism (defined as TSH > 5.5μIU/ml with normal free T4 and free T3) were considered as cases, and women without subclinical hypothyroidism were considered as controls. Laboratory measurements and clinical assessment was carried out in all the participants.

Exclusion criteria

Those with Known thyroid disease History of neck irradiation Chronic renal failure Severe illness (such as infections , recent myocardial infarctions, severe heart failure or recent intensive care admission) Taking drugs such as beta-blockers, amiodarone, interferon –α were excluded.

MEASUREMENTS

Thyroid function test- Free T4, Free T3 and TSH levels were measured. Thyroid function test is done using the electro chemiluminescence method. The normal range for TSH is 0.30-5.50 μIU/ml, for Free T4 the normal range is 0.70-1.80 ng/dl, and for Free T3 it is 1.70-4.20 pg/ml. Clinical Assessments Participants were examined for the presence of goiter and symptoms of hypothyroidism.

ANALYTICAL METHODS

The following data were collected from the entire study group
Age Presence of Hypertension (defined as BP > 140/90 mm Hg on more than one occasion or the patient is known to be hypertensive) Diabetes mellitus (defined as fasting blood sugar >126 mg% on two consecutive readings one month apart or the patient is known to be diabetic) Ischemic heart disease (defined as angina or myocardial infarction by self report or by analysis of standard 12 lead ECG for ischemic heart disease changes) Comparison between cases (subclinical hypothyroidism) and normal control subjects of similar age and ethnic group was done with regard to presence of IHD ,Hypertension and Diabetes mellitus.

STATISTICAL ANALYSIS

Statistical analysis was done using the statistical package for social sciences (SPSS).Different statistical methods were used as appropriate. Mean ± SD was determined for quantitative data and frequency for categorical variables. The independent t- test was performed on all continuous variables. The normal distribution data was checked before any t-test. The Chi-Square test was used to compare group difference for categorical variables. In logistic regression models, age was adjusted for estimation of each or all the independent effects of hypertension, ischemic heart disease and diabetes mellitus . A p- value < 0.05 was considered significant.

RESULTS

100 women above the age of 50 years who visited the medical outpatient clinic during the study period were studied 23 women were found to have the criteria set for the definition of subclinical hypothyroidism which meant a rate of 23%. Patients with subclinical

hypothyroidism were regarded as cases and remaining 77 patients were the control group.

There were differences in the mean age distribution among cases and controls are shown in table

Age in years	Patients with SCH	Patients without SCH
50-59	7	36
60-69	9	24
70 and above	7	17

There were 43 patients in the age group 50-59 of which 7 (19.44%) were having subclinical hypothyroidism .

In the 60-69 age group there were 33 patients of which 9 (27.27%) were having subclinical hypothyroidism.

In the 70 and above age group there were 24 patients of which 7 (29.17%) were having subclinical hypothyroidism.

The mean TSH level in patients with subclinical hypothyroidism was 12.11µIU/mL. For FT4 it was 1.03ng/dl and for FT3 it was 2.76pg/ml . There were differences in FT4, FT3, TSH distribution in cases and control as shown in Table

Mean	Patients with SCH	Patients without SCH
FT3(pg/ml)	2.76	3.01
FT4(ng/ml)	1.03	1.14
TSH (uIU/ml)	12.11	3.75

There were 23 patients with TSH level more than 5.5 µIU/ml, the upper level of normal range (0.30-5.5 µIU/ml). They are the subclinical hypothyroid patients in this study. Of those 23 patients 15(65.2%) had TSH level between 5.5 to 10 µIU/ml. The remaining 8 (34.8%) patients had TSH levels more than 10 µIU/ml as shown in the following Table

TSH levels in patients with SH

TSH levels in uIU/ml	No of patients
5.5 - 10	15 (65.2%)
>10	8 (34.8%)

Hypothyroid symptoms were reported in 7 out of 23 (30.43%) patients with subclincal hypothyroidism. Fatigability and constipation were the most common complaint, followed by weight gain .The frequency of hypothyroid symptoms in the subclinical hypothyroid patients are as shown in the table

Frequency of hypothyroid symptoms in patients with SH

Fatigability	6 (26.1%)
Constipation	6 (26.1%)
Weight gain	4 (17.4%)
Goiter	2 (8.7%)
Others(cold intolerance, hair loss etc)	2 (8.7%)

Goiter was present in 2 out of 23 patients with subclinical hypothyroidism (8.7%) and 5 out of 77 patients without subclinical hypothyroidism (6.5%). Other symptoms like cold intolerance hair loss were present in 2 of the 23 patients (8.7%) with subclinical hypothyroidism and 1 of the 77 patients (1.3%) without subclinical hypothyroidism.

The incidence of risk factors like hypertension diabetes and ischemic heart disease were compared between patients with subclinical hypothyroidism and control. They were analysed independently with Chi-Square test. The p- value showed that patients with subclinical hypothyroidism were significantly associated with ischemic heart disease compared to controls. The p- value is not significant for hypertension and diabetes. This is shown in table

Risk	Patients with SCH	Patients without SCH	p- value
Ischemic heart disease	5 (21.71%)	5 (6.5%)	0.047
Diabetes mellitus	4 (17.4%)	16 (20.1%)	0.490
Hypertension	6 (26.1%)	21 (27.3%)	0.570

DISCUSSION

Sub clinical hypothyroidism is highly prevalent in elderly women. A prevalence of 11 – 26 % had been reported in previous studies[24,25] our study shows a prevalence of 23 % in concordance with the other studies. Surveys that stratified TSH levels indicate a predominance of TSH < 10µIU/ml , which accounts for about 55-85% of cases. [27,28]. Almost 65% of our patients with subclinical hypothyroidism had TSH levels < 10µIU/ml. Studies that have reported thyroid antibody test on subjects with elevated TSH demonstrated seropositivity rates from 20-78%.[27,28]. Several studies have suggested that mild symptoms of hypothyroidism are more prevalent in patients with subclinical hypothyroidism than in age matched controls[29]. Fatigability and weight gain were the most frequent symptoms, 30% of our patients with subclinical hypothyroidism had symptoms of which fatigability (26%) and constipation (26%) were the most common There have been three published randomized prospective placebo controlled trials for the therapy of symptoms in patients with subclinical hypothyroidism. (30,31). Two trials reported significant improvement in symptoms of hypothyroidism. Case control and cross-sectional studies on association between subclinical hypothyroidism and cardiovascular disease have been done, but results were controversial. A 20 year follow up study of the original Whickham survey[5] showed no association between elevated TSH and increased risk of IHD, while a report of 1149 women from Rotterdam[32] showed increases atherosclerotic vascular disease and myocardial infarction in patients with with subclinical hypothyroidism. The present study showed a significant increase in Ischemic heart disease in patients with subclinical hypothyroidism compared with controls (p value of 0.047). Several studies on association between subclinical hypothyroidism and dyslipidemia have been done. The initial Whickham study[5] observed that lipid levels were not associated with TSH elevation after age adjustment. The Colorado study[25] and others noted a significantly elevated LDL cholesterol in subjects with subclinical hypothyroidism. Women with subclinical hypothyroidism did not differ from controls with regard to hypertension and diabetes in previous studies[12] The present study also showed it to be true.

CONCLUSION

Subclinical hypothyroidism is highly prevalent in elderly women above the age of 50 years Most of those with subclinical hypothyroidism have TSH level below 10µIU/ml Hypothyroid symptoms are prevalent in patients with subclinical hypothyroidism. (30% of patients in this study) Fatigability and Constipation being the most common symptoms Patients with subclinical hypothyroidism are more prone to develop ischemic heart disease There is no increased risk for developing hypertension and diabetes mellitus in patients with subclinical hypothyroidism Since subclinical hypothyroidism significantly increases the risk of ischemic heart disease as per our study it is necessary to screen the general population for the presence of subclinical especially in older age group. But whether to initiate treatment with levothyroxine is still a controversy[32]. Presence of risk factors such as older age, persistent elevation of TSH above 10 mlIU/l, presence of cardiovascular risk factors and positive Thyroid peroxidase antibody necessitates therapy with levothyroxine. The goal of therapy is to normalize TSH levels.

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