

Original Research Article

A hospital based cross sectional study on subclinical hypothyroidism in females over fifty years of age and its relation to hypertension, diabetes mellitus and ischemic heart disease at a tertiary care hospital, Hyderabad

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ABSTRACT

Background: Prevalence of subclinical hypothyroidism is more common in females compared to males and elderly age group. More studies are required to throw light on these aspects especially among elderly women with subclinical hypothyroidism and its association with prevalence of hypertension, diabetes and ischemic heart disease (IHD) among these women. The objective was to study prevalence of subclinical hypothyroidism among elderly females and its relation with the diabetes, hypertension and IHD.

Methods: Hospital based cross-sectional study was carried out among 178 women of 50 years and more. Detailed history, clinical examination and routine investigations were carried out. Free T4, free T3 and TSH (thyroid stimulating hormone) levels were measured using electro chemiluminescent method. Presence of hypertension, diabetes mellitus, IHD was noted.

Results: Prevalence of subclinical hypothyroidism was 24.7% and more in 61-70 years (38.5%). In 55% of the women the symptoms were absent. The most common symptom was fatigability and constipation. The prevalence of IHD among women with subclinical hypothyroidism was 22.7% compared to only 7.5% in women without subclinical hypothyroidism and this difference was found to be statistically significant ($p < 0.05$). For hypertension and diabetes, it was observed that the prevalence of these two conditions was slightly more in women without subclinical hypothyroidism but the difference was not found to be statistically significant ($p > 0.05$).

Conclusions: Prevalence of subclinical hypothyroidism in the elderly women was high. Subclinical hypothyroidism was found to be significantly associated with IHD but not with hypertension and diabetes.

Keywords: Subclinical hypothyroidism, Age, Relation, Diabetes, Hypertension

INTRODUCTION

A person presenting with raised TSH levels but with normal T3 and T4 levels is categorized as having subclinical hypothyroidism. Alternatively, it is also known as persons with decreased reserve of the thyroid or early thyroid failure or mild form of the hypothyroidism or preclinical hypothyroidism. The TSH levels in such cases

range from 4-15 μ IU/ml, a modest increase in the TSH levels. But there are cases when the TSH is >10 μ IU/ml and the T4 is reduced and they may present with few of the symptoms of the hypothyroidism.¹

Hashimoto's disease may sometimes be preceded with the subclinical hypothyroidism. Especially in elderly women it can occur in 7-10% of the cases.² Subclinical hypothyroidisms can be caused by either endogenous or

exogenous causes. The endogenous causes can be sub-acute thyroiditis, chronic autoimmune thyroiditis and the exogenous causes can be inadequate therapy with the thyroid replacement, effect of antithyroid drugs, thyroidectomy. Subclinical hypothyroidism is rather common than thought.²

A prevalence of 7.5% for females and 2.8% for males was documented in a study done at English county of Whickham among adults which was a population-based study.³ Prevalence of subclinical hypothyroidism is more common in females compared to males. It is also more prevalence in elderly people compared to the younger. The more prevalence in elderly and in females is attributed to the more levels of thyroid peroxidase and thyroglobulin in this sub-set of the population.^{1,4}

Natural history of this disease is well understood. 5.5% of the people spontaneously become euthyroid after one year.⁵ 7.8% to 17.8% progress to overt hypothyroidism.^{5,6} Studies show that 30% of cases can develop overt hypothyroidism within ten years and the risk was found to be directly proportional to the TSH levels.^{5,7} Subclinical hypothyroidism affects the lipid profile, heart, nervous system and can lead to the dysfunction of the mental system. It can also have an increased risk of the coronary heart disease and atherosclerosis.^{7,8} But other studies did not find this association as statistically significant.^{9,10} This difference between the studies can be attributed to their small sample size. Long term follow studies are also rare. Hence it cannot be said with confidence that cardiovascular system is affected by the subclinical hypothyroidism.

In previous studies it was observed that the women with subclinical hypothyroidism were similar to women without the disease in terms of body mass index, presence of diabetes and presence of hypertension.^{11,12}

Hence more studies are required to throw light on these aspects especially among elderly women with subclinical hypothyroidism and the prevalence of hypertension, diabetes and IHD among these women. With this background, present study was carried out to study the prevalence of subclinical hypothyroidism among elderly females and its relation with the diabetes, hypertension and IHD.

METHODS

The study site was the department of general medicine, Malla Reddy institute of medical sciences and hospital, tertiary care teaching hospital in Hyderabad. The study duration was from January 2016 to June 2017. The study conducted was a hospital based cross-sectional study. Women above the age of 50 years attending medical outpatient clinic of Malla Reddy institute of medical sciences and hospital, Hyderabad, which is a tertiary care centre, were included in the study based on inclusion and exclusion criteria.

Sample size

A sample of 178 women was randomly selected. From the previous studies, maximum prevalence was found to be 35% for subclinical hypothyroidism.^{3,4} Considering this percentage to calculate the sample size, 35% and taking allowable error as 20% with 95% confidence interval the sample size came out to be 178.

Inclusion criteria

Women above age of 50 years with TSH >5.5 μ IU/ml with normal free T4 and free T3 were considered as having subclinical hypothyroidism and rest as without subclinical hypothyroidism were included in the study.

Exclusion criteria

Patients with known thyroid disease, patients with history of neck irradiation, patients with chronic renal failure, bed ridden patients and those having associated severe comorbidities and patients on treatment with agents like as interferon- α , amiodarone, beta-blockers were excluded from the study.

Ethical considerations

Institution ethics committee permission was taken before the study was initiated. Patients diagnosed with subclinical hypothyroidism were asked to give the written informed consent after explaining the nature of the study and maintaining the confidentiality. All participants were treated as per the standard guidelines.

Written informed consent was taken from all eligible participants as per the inclusions and exclusion criteria.

Detailed history and general physical examination were performed as per proforma. Routine investigations like Hb, TLC, DLC, ESR, FBS, blood urea, serum creatinine, serum electrolytes (Na⁺, K⁺) were performed. Thyroid function tests free T4, free T3 and TSH levels were measured using the electro chemiluminescent method. The normal range for TSH is 0.30-5.50 μ IU/ml, for free T4 the normal range is 0.70-1.80 ng/dl and for free T3 it is 2.2-4.40 pg/ml. 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), IHD (defined as angina or myocardial infarction by self-report or by analysis of standard 12 lead ECG for IHD changes) was noted.

Statistical methods

Statistical analysis was done using the Microsoft office excel 2007. Different statistical methods were used as appropriate. Mean \pm 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 analyse group difference for categorical variables. In logistic regression models, age was adjusted for estimation of each or all the independent effects of hypertension, IHD and diabetes mellitus. P<0.05 was considered significant.

RESULTS

Table 1 shows prevalence of subclinical hypothyroidism among the study participants. The prevalence of subclinical hypothyroidism in the present study was found to be 24.7%. Given the hospital settings of the present study, this prevalence might have been little higher compared to the population-based studies.

Table 2 shows age distribution, free thyroxin (FT) levels in study participants with relation to subclinical hypothyroidism. The prevalence of subclinical hypothyroidism was more in the age group of 61-70 years (38.5%) followed by women above 70 years of age and less in women in the age group of 50-60 years (19.4%). Normal levels of FT3 and FT4 were more in women

without subclinical hypothyroidism compared to women with subclinical hypothyroidism. But these differences were not found to be statistically significant (p>0.05).

Table 3 shows TSH levels and symptom status in patients with subclinical hypothyroidism. Modest TSH levels were more common in 65.9% of women and 34.1% of women shown TSH levels more than 10 µIU/ml. In 55% of the women the symptoms were absent. The most common symptom was fatigability in 25% of the cases followed by constipation in 22.7% of the cases.

Table 4 shows association between subclinical hypothyroidism and presence of IHD, hypertension and diabetes. The prevalence of IHD among women with subclinical hypothyroidism was 22.7% compared to only 7.5% in women without subclinical hypothyroidism and this difference was found to be statistically significant (p<0.05). For hypertension and diabetes, it was observed that the prevalence of these two conditions was slightly more in women without subclinical hypothyroidism but the difference was not found to be statistically significant (p>0.05).

Table 1: Prevalence of subclinical hypothyroidism among the study participants.

Type of hypothyroidism	Number	%
Subclinical hypothyroidism	44	24.7
Without subclinical hypothyroidism	134	75.3
Total	178	100

Table 2: Age distribution, free thyroxin (FT) levels in study participants with relation to subclinical hypothyroidism.

Variables	Patients with subclinical hypothyroidism		Patients without subclinical hypothyroidism		Total		Chi square	P value	Interpretation
	N	%	N	%	N	%			
Age (in years)	50-60	21	19.4	87	80.6	108	5.592	0.061	Not significant
	61-70	15	38.5	24	61.5	39			
	>70	8	25.8	23	74.2	31			
FT4, FT3 normal levels	FT3	40	26.3	112	73.7	152	0.112	0.739	Not significant
	FT4	44	24.7	134	75.3	178			

Table 3: TSH levels and symptom status in patients with subclinical hypothyroidism (N=44).

Variables	Number	%	
TSH level in µIU/ml	5.5-10	29	65.9
	> 10	15	34.1
Symptoms of hypothyroidism	Present	20	45
	Absent	24	55
Symptom frequency	Fatigability	11	25
	Constipation	10	22.7
	Weight gain	7	15.9
	Goitre	3	6.8
	Other	4	9.1

Table 4: Association between subclinical hypothyroidism and presence of IHD, hypertension and diabetes.

Diseases		Patients with subclinical hypothyroidism		Patients with subclinical hypothyroidism		Chi square	P value	Significance
		N	%	N	%			
IHD	Present	10	22.7	10	7.5	6.284	0.006	Significant
	Absent	34	77.3	124	92.5			
Hypertension	Present	12	27.3	39	29.1	0.0016	0.483	Not significant
	Absent	32	72.7	95	70.9			
Diabetes	Present	08	18.2	29	21.6	0.076	0.391	Not significant
	Absent	36	81.8	105	78.4			

DISCUSSION

A prevalence of 11-35% had been reported in previous studies.¹⁻⁴ Our study showed a prevalence of 24.7% in concordance with the other studies. Surveys that stratified TSH levels indicate a predominance of TSH <10 µIU/ml, which accounts for about 55-85% of cases.^{13,14} Almost 65% of our patients with subclinical hypothyroidism had TSH levels <10 µIU/ml. Studies that have reported thyroid antibody test on subjects with elevated TSH demonstrated sero-positivity rates from 20-78%.^{3,6,15} Several studies have indicated in the past that odds of mild hypothyroidism symptoms were more in cases compared to the controls.¹⁵

Fatigability and weight gain were the most frequent symptoms in the present study, but not all studies have found this to be true.¹⁶ In the present study, 30% of our patients with subclinical hypothyroidism had symptoms of which fatigability (25%) and constipation (22.7%) were the most common. There have been three published randomized prospective placebo-controlled trials for the therapy of symptoms in patients with subclinical hypothyroidism.^{12,17} Two trials reported significant improvement in symptoms of hypothyroidism, whereas the third found no benefit of therapy.^{17,18} The benefit of therapy was related to TSH level, being more in those who have mean TSH level greater than or equal to 12.7 µIU/ml at baseline.^{13,16} In women with subclinical hypothyroidism and ovulatory dysfunction, thyroxin therapy may restore fertility.¹⁹

Various studies in the past were carried out to study the relation between subclinical hypothyroidism and the presence of IHD, but some reported positive association whereas some reported negative association.^{9,10,20,21} No association was found between subclinical hypothyroidism and IHD in a prospective of 20 years conducted at Whickham.²² But a study at Rotterdam done on 1149 women found a positive association.²¹ We also found that the prevalence of IHD among women with subclinical hypothyroidism was 22.7% compared to only 7.5% in women without subclinical hypothyroidism and this difference was found to be statistically significant (p<0.05).

Several studies on association between subclinical hypothyroidism and dyslipidemia have been done. The initial Whickham study observed that lipid levels were not associated with TSH elevation after age adjustment.³ The Colorado study and others noted significantly elevated LDL cholesterol in subjects with subclinical hypothyroidism.^{23,24}

A report from Rotterdam noted that with subclinical hypothyroidism subjects actually had lower total cholesterol.¹⁵ Women with subclinical hypothyroidism did not differ from controls with regard to hypertension and diabetes in previous studies.^{16,21} The present study also showed it to be true. There is documented evidence that many (but not all) effects are improved or corrected when L-thyroxin replacement is instituted. Levothyroxine treatment was recommended for majority of patients with mild thyroid failure, particularly those with symptoms, goitre, positive thyroid antibodies and those who are pregnant.²⁵ However, despite these positive indications that treatment carries some benefits, the benefits risk ratio of treatment remains to be determined, given the lack of outcome data and the considerable risk of TSH suppression in patients on Levothyroxine replacement.

Limitations

This study was limited to a single centre, only 178 patients were taken for the study and as this study had been carried out over a limited period of time with a limited number of patients, it could not have been large enough to be of reasonable precision.

CONCLUSION

There was a high prevalence of subclinical hypothyroidism in the elderly women in the present study with most cases having mild increase in TSH levels and one third presenting with symptoms. Subclinical hypothyroidism was found to be significantly associated with ischemic heart disease but not with hypertension and diabetes.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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