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A cross sectional study on subclinical hypothyroidism in adults in thanjavur medical college

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ABSTRACT

Background: Subclinical hypothyroidism is a very common disorder with prevalence ranging from 1–10% of the, mostly adult, population, with the highest rate of about 26% in elderly women. Clinically subclinical hypothyroidism manifests as dyslipidemia, heart disorders, and neurological disorders and mental problems, and several many cross-sectional studies have also postulated that it confers an increased risk of atherosclerosis

Materials and Methods: Adults above 18 years of age attending Medical outpatient clinic of Thanjavur medical college and hospital from the period of January 2019 to January 2020 were included in the cross sectional study. The sample included about 218 adults whom were selected randomly.

Adults with a known thyroid disorder, previously treated for thyroid disorder, patients having clinical infectious disease and adults with comorbidities of Diabetes mellitus, Hypertension, Coronary artery disease,and chronic kidney diseases were excluded.

Results: Our study shows a prevalence rate of 12.4 % for subclinical hypothyroidism in elderly. Considering those observations our study demonstrated most of the patients (30.4%) with subclinical hypothyroidism showed symptoms of thyroid hormone deficiency among which fatigability(32.3%) and constipation (31.3%) were the most frequently seen. the study showed a significant raise in autoimmunity in elderly women with subclinical hypothyroidism compared with other controls.

Conclusion: Subclinical hypothyroidism, a common condition, is prevalent in 12.4% of the population, with higher rates in females and elderly women, and is characterized by fatigability and constipation.

1. Introduction

The term subclinical hypothyroidism was originally used to describe a condition in which the patient has a low-normal free T4 but a slightly elevated serum TSH level. The other terms that can be used for this condition include are mild hypothyroidism, decreased thyroid reserve, early thyroid failure etc. Such patients just have modest elevation in Thyroid Stimulating Hormone levels, with levels fall typically between 4 and 10 microIU/L.

Hypothyroidism is usually found to be much higher in females than males. And also the frequency increases with age. The overall prevalence is being reported to fall between 4–10% in most of the large general population screening surveys[1–4] and in the elderly it raises to 7–26% from the studies conducted among the elderly.[1,2,5–10] Subclinical hypothyroidism is commonly seen in patients whom they develop clinical hypothyroidism in a later period. These patients with time will present with full clinical picture and classic symptoms of clinical hypothyroidism.

Various Studies have shown increased vascular tone at rest and left ventricular systolic dysfunction with exercise, slowed left ventricular relaxation time and impaired endothelial function in thyroid disorders. Some studies have shown positive effect such as improvement of systolic

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time interval for heart and increase in cardiac contractility with levothyroxine therapy. Patients with subclinical hypothyroidism have common symptoms like poor memory, cognition defects, dry skin, fatigue, weakness in muscles, cramps, puffiness of eyes, cold intolerance, hoarseness and constipation. Findings like improper peripheral nerves functioning that can be characterized by reduced amplitude and problems with reflexes also has been found. Any Woman who is pregnant or those planning for pregnancy, if presents with subclinical hypothyroidism must be treated with levothyroxine hormone to bring TSH in the normal range and the TSH level should be maintained at the lower limits. This is because the fact that high maternal Thyroid Stimulating Hormone can cause neuro-psychological complications or increased fetal wastage in the offspring. There are no standardized interventional trials to assess the benefits of replacement of thyroid hormone in this special population.The prescription levothyroxine therapy is justified by its potential risk-benefit ratio. [11–33]

2. Materials and Methods

2.1. Study design and enrolment criteria

The study was a cross-sectional epidemiology study conducted at Thanjavur Medical College, focusing on the prevalence of hypothyroidism. The study assessed hypothyroidism prevalence through thyroid hormone measurements, self-reported and undetected hypothyroidism, sub-clinical hypothyroidism, and anti-thyroid peroxidase antibody positivity. The study included all male and female natives aged 18 years and above, with participants excluded if they were pregnant, had systemic illnesses, or were taking drugs that interfered with thyroid function tests. The study was approved by a Central Ethics Committee. The study required all participants to provide written informed consent prior to enrolment.

2.2. Study procedure

Prior to enrollment, participants completed a medical history evaluation, a general physical examination (which included a thyroid gland examination and anthropometry), and laboratory tests. The haematological and biochemical examinations were carried out by a centrally accredited laboratory. Thyroid hormone (FT3, FT4, and TSH) assays were run on the automated immunoassay analyzer using the chemiluminescence method. Immulite 2000 was used to conduct an enzyme-linked immunosorbent test (ELISA) to assess anti-TPO antibodies.

Participants were categorised using the following definitions according to their current thyroid function test findings and previous thyroid history: Serum-free thyroxine (FT4) <0.89 ng/dL and thyroid stimulation hormone (TSH) >5.50 μU/mL are signs of hypothyroidism. Serum FT4 >1.76 ng/dL and TSH <0.35 μIU/mL indicate hyperthyroidism. TSH >5.50 μIU/mL and normal serum FT4 indicate subclinical hypothyroidism. Subclinical hyperthyroidism: TSH <0.35 μIU/ml and normal serum FT4 levels Hypothyroidism that was self-reported by the subjects: those who had a history of the condition and were taking levothyroxine. Undetected Hypothyroidism: Subjects with hypothyroidism who had no prior history of the condition and who had abnormal thyroid function tests. Positive for anti-TPO antibodies means having levels higher than 35 μIU/ml.

2.3. Statistical analysis

With the aid of SAS® for Windows, statistical analysis was carried out. The analysis was done on the group of all eligible participants who had signed up for the study in accordance with the protocol. As counts and percentages, the prevalence of hypothyroidism and other thyroid problems was presented. The prevalence of hypothyroidism among various age groups and gender categories was examined using a Chi-square test. Using the dependent variable "whether the subject has hypothyroidism or not" and the independent variables "Age" and "Gender," multiple logistic regression was used to describe factors related to hypothyroidism. Analyses of SCH and anti-TPO antibody positivity were carried out similarly.

3. Results

About 218 volunteers above 18 years of age who attended the medical outpatientclinic in Thanjavur medical college (TMCH) and hospital during the period of January 2019 to January 2020 were included in the study and data collected with getting consent. Out of 218 adults 27 of them were found to have fulfil the aforementioned criteria set for the definition of subclinical hypothyroidism (SH). The rate is about 12% out of 218 cases. Patients with subclinical hypothyroidism were regarded as cases and remaining 191 patients were included in the control group.Table 1

Table 1: Distribution among cases and controls according to age group

Age group	Individuals without SH	Individuals with SH
20-29 years	18.3 -34	11.1 - 3
30-39 years	33- 64	33 - 9
40-49 years	20.9 – 40	18.5 -5
50-59 years	19.4 – 37	33.3 -9
60 and above	8.4 – 16	3.7 - 1

Among the 37 patients in 20-29 age group 3 (11.1%) of them had subclinical hypothyroidism. Among the 73 patients in 30-39 age group 9 (33.3%) of them had subclinical hypothyroidism. Among the 45 patients in the age group of 40 -49, 5(33.3%) of them had subclinical hypothyroidism. Among 46 patients in 50-59 age group

9(33.3%) included under subclinical hypothyroidism. Out of 17 patients in 60and above group 1(3.7%) included under subclinical hypothyroidism. The mean Thyroid Stimulating Hormone (TSH) level in patients with SH is 6.8 microIU/ml. For Free T4 it was around 1.01 ng/dl and for Free T3 it was about 3.3 pg/ml. Differences in Free T4, Free T3, Thyroid Stimulating Hormone, Thyroid Peroxidase.Table 2

Table 2: Antibodies distribution were seen among cases and controls.

Mean	Individuals without SH	Individuals with SH
TSH (microIU/ml)	3.2	6.8
FT3 (pg/ml)	3.14	3.3
FT4 (ng/ml)	0.969	1.01
TPO (IU/ml)	3.2	16.3

There were 27 patients with Thyroid Stimulating Hormone level more than 4.25 microIU/ml and the upper level of normal range is considered as 0.30-4.25microIU/ml. They are the subclinical hypothyroidism (SH) patients in our study. Among them Symptoms of hypothyroidism were seen in 6 out of 27 (28.57%) patients with subclinical hypothyroidism and the most recurrent complaints were fatigability and constipation, further followed by weight gain.

The frequency of distribution of hypothyroid symptoms in the subclinical hypothyroid patients are as follows in the Table 3.

Table 3: Frequency of hypothyroid symptoms in patients the study

Constipation	7 (3.2%)
Fatigability	7 (3.2%)
Weight Gain	4 (1.8%)
Cold intolerance	4 (1.8%)
Goitre	5(2.3%)
Others (Infertility etc)	3 (1.4%)

Presence of goitre is in about 5 out of 27 patients with subclinical Hypothyroidism and other symptoms like cold intolerance, infertility were present in about 7 out of 27 patients with subclinical hypothyroidism. The gender wise distribution of individuals is Andover all frequency increased in females. Thyroid auto antibodies(TPO) present in increased frequency in females that too having high prevalence in elderly females.They were analyzed and calculated individually with chi-Square test and p- value showed that patients with subclinical hypothyroidism were significantly associated with increased association of autoimmunity in elderly females.

A study involving 218 volunteers aged 18 and above from January 2019 to 2020 found that 27 of them had subclinical hypothyroidism (SH), a condition affecting about 12% of the 218 cases. The mean TSH level in SH patients was 6.8 microIU/ml, with the upper normal range being 0.30-4.25 microIU/ml. Symptoms of SH included fatigability, constipation, weight gain, goitre, cold intolerance, and infertility. The frequency of SH was higher in females, with thyroid auto antibodies (TPO) being more common in elderly females. The study found that patients with SH were significantly associated with increased autoimmunity in elderly females, indicating a higher prevalence of SH in these groups.In this study, investigation concluded that 12.4% of the population under study has subclinical hypothyroidism. About 17% more females than males have subclinical hypothyroidism. Subclinical hypothyroidism with autoimmunity is more common in elderly ladies. The most frequent signs of subclinical hypothyroidism were agitability and constipation.

4. Discussion

Subclinical hypothyroidism has very high prevalence among elderly women. The prevalence in elderly aged people usually falls between 7 – 26 % in various studies [1,2,5–10] with an increased rate that reaches to 26% in elderly females. [6,10,34–42]

Our study shows a prevalence rate of 12.4 % which is also shows similar results in concordance with other Studies. Many large number surveys and analyses have come to a conclusion that the percentage of cases with Thyroid Stimulating Hormone (TSH) < 10microIU/ml are cases of subclinical hypothyroidism is around 55-85%. [6,10,39] About 66.67% of our cases with subclinical hypothyroidism had TSH levels < 10microIU/ml. Many other observations have shown the same results that the thyroid antibody (TPO) test done on these patients with increased thyroid stimulating hormone (TSH) turned out to be positive. [6,10,39] Some other observations have also shown that nearly 1/3rd of the patients with subclinical hypothyroidism have symptoms of deficiency of thyroid hormones. [2] Fatigability and weight gain were the most common symptoms among various other symptoms, but not all observations have said the same to be true. [5] Considering those observations our study demonstrated most of the patients (30.4%) with subclinical hypothyroidism showed symptoms of thyroid hormone deficiency among which fatigability(32.3%) and constipation (31.3%) were the most frequently seen.

With the supporting evidence of the above observations a study has been conducted in Switzerland with a large number of females about 300 subjects were evaluated. Among those subjects 93 patients were found to have subclinical hypothyroidism and about 24% of them presented with symptoms that are commonly seen in hypothyroidism. These findings give the impression that it's not so easy to tell a case of primary hypothyroidism by simply seeing the symptomatology and thyroid profile alone. And also those patients who came with normal

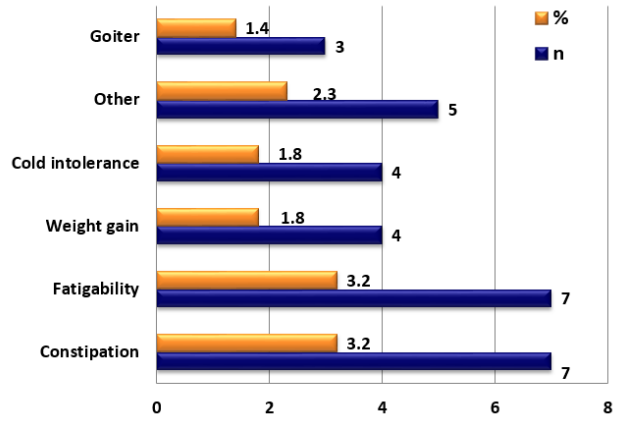

Figure 1: Frequency distribution of type of symptoms of hypothyroidism observed in the study (N=218)

thyroid status and those presented with subclinical hypothyroidism cannot be easily picked up only based on symptoms.

Although these studies shows some important statistics with significance in many number of people, but when a single patient is considered it is very difficult to separate a person who presents with normal hormone levels from another person who comes with either having hypothyroidism or subclinical hypothyroidism.

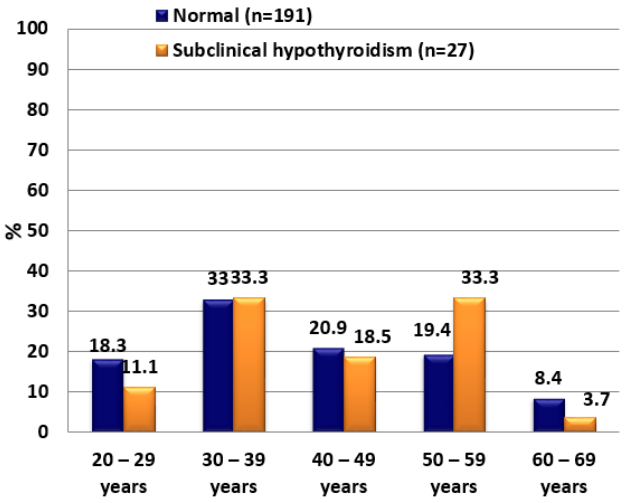

Figure 2: Comparison of age category with respect to the occurrence of subclinical hypothyroidism observed in the study.

There are about 5 studies which have shown that there is improvement in psychological and mental health when symptoms associated with SH. And also improvement in quality of life is also reported. From the many aforementioned studies only two have shown results that there is improvement, while the average thyroid stimulating hormone values were above 11 microIU/L. One of the above studies showed only a mild but significant benefit in the form of difference in the rate of response in the range of 24% when the same is compared with the placebo whereas the other group treated with thyroxin hormone.In addition to this nonfactors could show who will gain from thyroid hormone replacement therapy. But there was no advantage of thyroid hormone therapy shown by the 2 studies which were remaining to be checked. Among these two studies one of them showed improvement in cognition which is seen as improvement in memory scores due to therapy on comparison to placebo while the other study failed to show the same. Since very few symptoms relating to thyroid hormone deficiency were made out in the group which has been treated with thyroid hormone and those treated with placebo and also patients who were in the range of 5-10 mU/L thyroid stimulating hormone were not very sure whether they should be prescribed with thyroid hormone therapy or placebo. Considering all these results from the trials said above we can come to a conclusion that 1) Patients with Thyroid Stimulating Hormone between 5 to 10 microIU/litre did not gain significantly if they doesn't have symptoms, from thyroid hormone therapy than the patients who were prescribed placebo 2) Among those subjects presenting with worse subclinical hypothyroidism only twenty five percent of them benfited from thyroxine hormone substitution therapy 3) Thyroid hormone replacement therapy is not indicated in the patients without symptoms on the fact that large number of people with SH have values of TSH that fall between 5 to 10 microIU/liter 4) Patient whom have subclinical hypothyroidism (SH) with TPO antibodies positivity i.e more than median range should be treated irrespective of symptoms. The treatment with thyroxin in those subjects with SH can show good results which is manifested by improvement of symptoms. In subjects with thyroid stimulating hormone between 5-10 microIU/ml there is a chance for observation or therapy to be started with regard to an individual patient situation which includes various factors. The relationship between subclinical hypothyroidism and coronary heart disease is still not clarified.[6]

The Busselton Health Study said that subclinical hypothyroidism is an independent risk factor for coronary heart disease. The Rotterdam Study[6] finally concluded that a higher prevalence of atherosclerotic coronary vascular disease in female subclinical hypothyroidism patients who were about 55 years of age or older than that. Razvi et al. also concluded from a meta-analysis showing that subclinical hypothyroidism has been linked with increased risk for coronary artery heart disease in peoples from younger populations only, but the degree of subclinical hypothyroidism can also play an important role. And also, the Wickham survey, a large-scale, long term follow-

up study, said that there is no significant evidence to suggest that subclinical hypothyroidism is associated with an increased risk of ischemic heart disease(IHD).[43]

Our present study showed a significant raise in autoimmunity in elderly women with subclinical hypothyroidism compared with other controls.

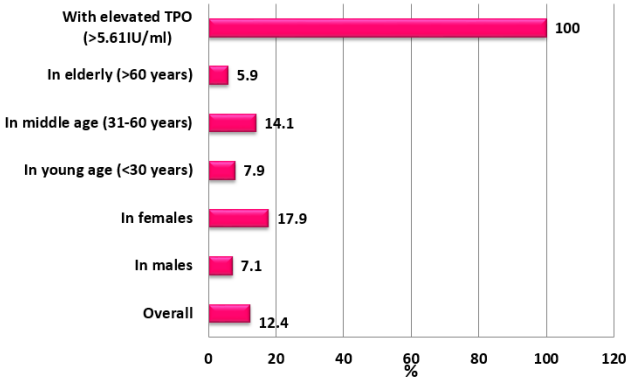

Figure 3: Incidence of subclinical hypothyroidism with respect to various conditions observed in the study

Many other observations on relation between subclinical hypothyroidism and dyslipidemia have also been conducted. A study conducted by Althaus et al.[44] found out that the quantity of low density lipoprotein (LDL) cholesterol was more while that for high densitylipoprotein cholesterol was less in patients presenting with this condition when they were compared with people who were normal thyroid hormone levels. These results were similar to other researchers (LDL-R) because lowdensity lipoprotein cholesterol receptor gene is a thyroid hormone responsive element (TRE) and is influenced by T3. So Goitre is two times common among in patients with subclinical hypothyroidism and it is observed in 3.5% of our patients. The normal distribution of serum Thyroid Stimulating Hormone values in the general population is usually skewed, where the majority of individuals having Thyroid Stimulating Hormone values recorded at the lower level.Some studies conducted in America found out that treating as well as screening subclinical hypothyroidism in all adults above the age of 35 years is much more cost effective.Subclinical hypothyroidism is very frequently encountered problem in the community in which patients can end ultimately in clinical hypothyroidism. Subjects coming with these hormonal imbalance usually presents with a number of somatic symptoms and also neurological deficits in areas related to memory and also cardiac problems also more prevalent like improper relaxation of the heart in during diastole and contraction during systole. Some individuals may present only with depressed mood and increase in the amount of total lipid and low density lipoprotein may be found out in further follow up testing which is predisposing the patient to the problem of landing him ultimately in atherosclerosis. There are various other observations which have demonstrated that many of these untoward effects can be cured if the patients are adequately treated with Levothyroxine hormone. From the above discussion the treatment should be started as early as possible in the disease even though these patients doesn't have symptoms because these patients will eventually lands up with the classical symptoms. Hence therapy should be started for most of the subjects presenting with subclinical hypothyroidism with special concern to those subjects presenting with symptoms, or having antibodies against the thyroid gland, those patients diagnosed first time during pregnancy The potential end results of untreated or inadequately treated SH may end on atherosclerosis in adults and can have an effect on intellectual potential in infants born to mothers with mild thyroid failure. It is no longer scientifically arguable whether mild thyroid failure is something or nothing. So more organized studies with proper randomization should be conducted to elucidate the ill effects of Subclinical Hypothyroidism and the effect of early treatment of the same.

5. Conclusion

The Prevalence of subclinical Hypothyroidism in the studied population is 12.4% with a higher prevalence of subclinical hypothyroidism in females about 17% and is characterized by fatigability and Constipation

6. Source of Funding

None.

7. Conflict of Interest

None.

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