Incidence of sub clinical thyroid dysfunction among asymptomatic adult population

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Abstract

Background: Patients with subclinical thyroid dysfunction are universally encountered in routine clinical practice. Advanced diagnostic techniques have created new categories of thyroid disorders such as subclinical hypothyroidism and hyperthyroidism. The management of subclinical thyroid dysfunction is controversial. Patients with subclinical thyroid dysfunction may have vague, nonspecific symptoms that do not aid the clinical apperception. This study aimed to screen the normal adult population for the incidence of subclinical thyroid dysfunction and discuss the optimal management strategy.

Materials and methods: Four hundred subjects with no clinical evidence of thyroid dysfunction were included in the present study. Elaborate history in the form of a symptom questionnaire was obtained and clinical examination was performed. Laboratory analysis of thyroid function was done by electrochemiluminescence immunoassay (ECLIA). Patients with normal free thyroxine (FT4) and triiodothyronine levels (T3) were further classified into subclinical hypothyroid based on the serum thyroid-stimulating hormone (TSH) levels. The incidence of subclinical thyroid disorder in the sample population was detected and optimal management strategies were followed as per the European thyroid association (ETA) guidelines.

Results: The normal TSH value by ECLIA was 0.27 - 4.2μIU/ml. Seventeen (4.25%) out of four hundred subjects included in the present study were found to have subclinical thyroid dysfunction. The Ratio of subclinical hypothyroid cases to subclinical hyperthyroid cases was found to be 12:5. Clustering of the cases was found around the age of 60 years and was significantly more common among females in comparison to males. Cases with subclinical thyroid dysfunction were managed by follow up after a thorough evaluation and treatment of other comorbid conditions.

Conclusions: The study provides valuable insight towards understanding the epidemiology and management of subclinical thyroid disorders in the present scenario. Screening is recommended for a
high-risk population since there is good evidence that subclinical thyroid dysfunctions may be associated with progression to overt disease in up to 5% of the population.

**Key words**
Subclinical, Hypothyroidism, Hyperthyroidism, Management.

**Introduction**

Subclinical thyroid dysfunction is defined as an abnormal level of serum thyroid-stimulating hormone (TSH) with normal free thyroxine (FT4) and triiodothyronine levels (T3) [1]. A study published by the American Academy of family physicians showed the prevalence of subclinical hypothyroidism as 4 to 8.5 percent and may be as high as 20 percent in women older than 60 years. Subclinical hyperthyroidism is found in approximately 2 percent of the population [2]. In the Indian scenario there is paucity of data regarding the prevalence, therapeutic management and screening guidelines of the condition [3].

Etiology of subclinical thyroid dysfunctions can be assessed by careful clinical evaluation. The causes for low serum TSH concentration include pregnancy, euthyroid sick syndrome or medications such as dopamine, glucocorticoids and dobutamine [4]. Serum TSH may be elevated in patients with nonfunctioning pituitary adenomas, central hypothyroidism, adrenal insufficiency and primary subclinical hypothyroidism [5-7].

The consequences of subclinical hypothyroidism include progression to overt hypothyroidism, atherosclerosis, coronary heart disease (CHD) and mortality by heart failure [8]. Some studies have recorded cognitive impairment in subjects with subclinical hypothyroidism that normalized after thyroxine replacement [9]. Subclinical hyperthyroidism may progress to overt hyperthyroidism, atrial fibrillation and reduced bone mineral density [2].

Most of the management guidelines recommend rechecking serum TSH, FT4, T3 and thyroid peroxidase antibodies within 3–6 months [3, 10]. This therapeutic stake is not to improve the clinical status of patients but to prevent the progression towards adversities.

**Materials and methods**

Present study was a cross sectional observational study that was conducted in the department of medicine of a tertiary care hospital between January 2016 and February 2017 in Hyderabad, Telangana. Four hundred asymptomatic subjects of age ≥ 18 years, with no clinical history of thyroid dysfunction were included in the study. Patients with known family history of thyroid dysfunctions, overt thyroid dysfunction on medication and newly diagnosed cases of obvious thyroid dysfunction were excluded from the study. Written informed consent was obtained from all subjects included in our study.

Detailed history was taken in the form of a symptom questionnaire. Complete clinical evaluation by physical examination was conducted to look for the thyroid enlargement, skin texture, weight loss/gain, pedal edema and ocular manifestations of thyroid dysfunctions. Electrocardiogram (ECG), plasma glucose, total cholesterol (TCHOL), high-density lipoprotein cholesterol (HDL-C), triglyceride levels and Mean Arterial blood Pressure (MAP) were recorded. Fasting venous blood sample was drawn from all subjects with aseptic precautions and serum/plasma samples were used to study the thyroid function tests (T3, FT4 and TSH). Thyroid function test, (TST) was based on the principle of electro-chemiluminescence.

Statistical analysis of the data was performed by SPSS statistical software (version 22) and statistical significance was calculated by percentage analysis and p-value interpretation. P values > 0.05 was considered insignificant and
values ≤ 0.05 was regarded as significant.

**Results**

Four hundred healthy subjects with no clinical history of thyroid dysfunction of age ≥ 18 were included in this study. Seventeen (4.25%) out of four hundred subjects included in the present study were found to have subclinical thyroid dysfunction.

Normal TSH values ranged from 0.27 - 4.2μIU/ml. Those cases with TSH > 4.2μIU but <10μIU/ml with normal T3, FT4 were considered subclinical hypothyroid subjects and those with TSH < 0.27μIU/ml with normal T3, FT4 were taken as subclinical hyperthyroid subjects. Twelve (3%) of the subjects had subclinical hypothyroidism with TSH > 4.2μIU/ml but < 10 μIU/ml (P value < 0.05) and five (1.25%) out of four hundred subjects had subclinical hyperthyroidism (Figure - 1).

Demographic data analysis showed an increased clustering of the cases around the age of 60 years as depicted in Figure - 2. Among the Seventeen cases of subclinical thyroid dysfunction eleven (64.70%) were females and six (35.29%) were males. Out of the Seventeen cases eight (47.05%) were absolutely asymptomatic (p value <0.05). The remaining cases presented with co-morbid clinical manifestations such as altered blood glucose profile, lipid profile, mean arterial pressure, pedal edema and ECG changes as depicted in Figure - 3. Medical treatment was initiated for hypertensive, diabetic patients, patients with altered lipid profile, ECG changes and pedal edema.

Based on ETA guidelines [11], patients with subclinical hypothyroidism were asked to repeat the thyroid profile along with thyroid peroxidase antibodies after 3 months. None of the patients progressed to overt hypothyroidism in the first quarter, however one patient (8.3%) was positive for thyroid peroxidase antibodies with TSH= 9μIU/ml and normal T3, FT4. All patients were put on yearly follow up at the end of the study period.

Risk versus benefit assessment was done in subclinical hyperthyroid patients. Since all the patients had borderline low TSH levels they were put on follow up after confirming the absence of co-morbidities such as atrial fibrillation and osteoporosis.

**Discussion**

Subclinical thyroid dysfunctions are diagnosed when peripheral thyroid hormone levels are within normal reference laboratory range but serum TSH levels are deranged. Thyroid hormone homeostasis is regulated as part of a negative feedback control circuit within the hypothalamic-pituitary-thyroid axis [12, 13].

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**Figure - 2**: Age distribution of the cases.

**Figure - 3**: Clinical presentation of the cases with subclinical thyroid disorders.
The incidence of subclinical hypothyroidism was 3% in comparison studies by Deshmukh, et al. [3] showed a prevalence of 11.5% in Mumbai. A study by the National Health and Nutrition Examination Survey [14] (NHANES III) of an unselected U.S population found subclinical hypothyroidism in 4.3% of the reference population.

Present study is in agreement with studies by Hoogendoorn, et al. [15] and Somwaru, et al. [16], which show that advancing age has direct correlation with the cases. Most of the studies [17, 18] show an increased female preponderance similar to our study. Therefore variables such as sex, age, race/ethnicity and geographic location clearly influence the presence of subclinical hypothyroidism in a given population.

Coming to subclinical hyperthyroidism, the present study gives an incidence of 1.25%. Studies by Marqusee, et al. [19] have shown a prevalence range of 0.7 and 12.4%. Similar to subclinical hypothyroidism findings, advancing age and female sex seems to have a higher association with subclinical hyperthyroidism.

The criteria for treatment of subclinical thyroid disorders are controversial and hence an individualized judgment is mandatory in order to evaluate the grade and the clinical consequences of the condition in a given patient [20, 21]. Present study based its treatment regimen on ETA recommendations [11, 22]. Factors such as absence or presence of anti-thyroid antibodies, cardiovascular risk factors and other co-morbidities influence treatment decisions. Minimal variations of TSH along with absence of other overt risk factors do not necessarily merit treatment, in such situations active surveillance is advised.

Conclusion
The study highlights the association of various variables such as age, sex and geography with the epidemiology of subclinical thyroid disorders. Screening of high-risk cases helps in early identification and thereby reduces the associated mortality and morbidity. Treatment of subclinical thyroid disorders in the present scenario is based on the evidence that subclinical thyroid dysfunctions may be associated with progression to overt disease. Hence individualized treatment and regular follow up is strongly recommended in the management of subclinical thyroid disorders.

Limitations of the study
Since the study period lasted for a year the follow up of the cases could not be documented in this study.

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