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A Study on Anti-Thyroid Peroxidase, Thyroxine, Tri-Iodothyronine and TSH in the Subclinical Hypothyroidism

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ABSTRACT: The aim of present study was to assess the efficacy of the case finding approach in identifying women with subclinical thyroid dysfunction. Single centre cohort study carried out at SRM Medical College Hospital and Research Centre, Kattankulathur and the statistical analysis was done by using student's *t*-test. A prospective analysis of Thyroxine (T4), Thyroid-stimulating hormone (TSH), Tri-iodothyronine (T3), and Thyroid Peroxidase antibodies (anti - TPO) was carried out in 15 patients and age-matched 15 normal women. Results of the study revealed subclinical hypothyroidism according to the TSH, T4 and T3 and the results of anti-TPO suggests subclinical hypothyroidism were going for autoimmune changes during the initial phase of the disease.
Key Words: Thyroid stimulating hormone, Tri-iodothyronine, Thyroxine, Thyroid Peroxidase antibodies.

INTRODUCTION

Hyperthyroidism and hypothyroidism are common conditions that have lifelong effects on health[1,2]. About 5% of U.S. adults report having thyroid disease or taking thyroid medication[1,2]. Hypothyroidism causes symptoms that reduce functional status and quality of life[3]. Subclinical thyroid dysfunction, which can be diagnosed by thyroid function tests before symptoms and complications occur, is viewed as a risk factor for developing hyperthyroidism and hypothyroidism complications[3]. The goal of screening is to identify and treat patients with subclinical thyroid dysfunction before they develop these complications. The terms *subclinical hypothyroidism* and *mild thyroid failure* refer to patients who have an elevated TSH and a normal FT4 level. Subclinical hypothyroidism is common, especially in older women[3,4].

Subclinical hypothyroidism is defined as a condition in which serum TSH concentration is above the statistically defined upper limit of the reference range when the serum free T4 concentration is within its reference range[1]. The prevalence of subclinical hypothyroidism is about 4 to 8.5 percent and may be as high as 20 percent in women older than 60 years[2]. Patients with a serum thyroid-stimulating hormone (TSH) level greater than 10 µIU/mL have a higher incidence of elevated serum low-density lipoprotein cholesterol concentrations; however, evidence is lacking for other associations[3].

In about 95 percent of cases, hypothyroidism is due to a problem in the thyroid gland itself and is called subclinical hypothyroidism. However, certain medications and diseases can also decrease thyroid

function[4].The symptoms of subclinical hypothyroidism vary widely; some people have no symptoms while others have dramatic symptoms or, rarely life-threatening symptoms[5]. Thyroid hormone normally stimulates the metabolism, and most of the symptoms of hypothyroidism reflect slowing of metabolic processes. General symptoms may include fatigue, sluggishness, weight gain, and intolerance of cold temperatures[6-7].

MATERIALS AND METHODS

ANTHOS *2020* ELISA Reader was obtained from Anthos Labtec Instruments, Austria. ELISA assay kits for TSH, T3, T4, free T3, free T4 and TPO were obtained from Adaltis Italia, Italy. All the reagents in the kit were calibrated for the direct determination of human thyroid hormones in human serum or plasma and not for the determination in saliva specimen.

We used a prospective cross sectional study design among the females. Fifteen healthy women and fifteen suspected patients, who attended SRM Medical College Hospital and Research Centre, Kattankulathur, have participated in the studies. The individuals were from in and around SRM University, Kattankulathur. The age group was above 40 years and in the range of 40 to 65 years (average body mass index is 25 kg/m²). They were not having goiter or previous/present thyroid diseases and no history of taking any medication. The concern was obtained from the participants before the commencement of the study. Blood sample were collected aseptically. Blood was allowed to clot; samples were centrifuged at 2000 rpm (revolution per minute) for 10 minute at room temperature. Serum was separated and was stored at -20°C until the analysis, to minimize non-specific variability of all parameters. The control group includes individuals with age ranging from 40-60 years for analyzing TSH, total T4 (tT4), total T3 (tT3), free T4 (fT4), free T3 (fT3) and anti-TPO. All the data in the text and tables were reported as the Mean ± Standard Deviation (SD). Comparisons among control subjects and subclinical hypothyroid patients were performed by the Student's *t*-test for unpaired data, using the software SPSS-Version-16.

RESULTS AND DISCUSSION

Thirty individuals who attended SRM Medical College Hospital and Research Centre, Kattankulathur were enrolled for the studies among them fifteen normal individuals were grouped as a control group. Fifteen individuals having the clinical complaints were grouped as test group with results of serum TSH level higher than 10 µIU/ml. The results of control and test are tabulated in **Tables No. 1** and **Table No. 2**.

Different levels in control group

The highest level of TSH is 4.6 µIU/ml and the lowest is 2.11 µIU/ml. The highest level of total T3 is 1.98 ng/ml and the lowest is 1.2 ng/ml. The highest level of total T4 is 152.8 ng/ml and the lowest is 90.3 ng/ml. The highest level of free T3 is 3.4 pg/ml and the lowest is1.5 pg/ml. The highest level of free T4 is 1.85 ng/dl and the lowest is 1.28 ng/dl. The highest level of anti-TPO is 66.0 IU/ml and lowest 35.0 IU/ml. **(See Table No. 1)**

Different levels in test group

The highest level of TSH is 24.0 µIU/ml and the lowest is 10.8 µIU/ml. The highest level of total T3 is 1.02 ng/ml and the lowest is 0.42 ng/ml. The highest level of total T4 is 180.0 ng/ml and the lowest is 58.0 ng/ml. The highest level of free T3 is 2.05 pg/ml and the lowest is 0.32 pg/ml. The highest level of free T4 is 1.9 ng/dl and the lowest is 0.78 ng/dl. The highest level of anti-TPO is 147.2 IU/ml and lowest 75.0 IU/ml. **(See Table No. 2)**

Statistical analysis

Using student's *t*-test it was found that the levels of TSH, tT3, fT3 and anti-TPO in the control group were statistically significant with the test group at 95% level of confidence (P Value is 0.05). But tT4 and fT4 were found to be in-significant. Our data shows that in subclinical hypothyroidism the level of tT4 and fT4 is normal within the limits. **(See Table No. 2)**

Data relating the progression of subclinical to overt hypothyroidism were assessed. The follow up study of Whickman cohort has found that individuals with a serum TSH >2 µIU/ml at their primary evaluation had an increased ratio of developing hypothyroidism over the next 20 years[8]. In majority of patients, thyroid disease symptoms are subtle in presentation so that only biochemical testing or cytopathologic evaluation can detect the disorder[9]. Individual variation in thyroid hormone test values together with twin studies suggests that each individual has fanatically determined fT4 set point[10].

Studies suggest that early identification and treatment of mild subclinical hypothyroidism may prevent the long term effects of low thyroid hormone levels. NACB (National Academy of Clinical Biochemistry) recommends upper limits of serum TSH euthyroid reference range will be reduced to 2.5 µIU/ml because normal euthyroid volunteers have serum TSH values between 0.4 µIU/ml to 2.5 µIU/ml[11].

Subclinical Hypothyroidism accompanied with normal fT4 and fT3 should be evaluated for TPO-Abs to rule out thyroid autoimmunity. The higher the TPO-Abs the more rapid the failure of thyroid. To validate these claims, present study has proposed to study the subclinical hypothyroidism[12-13]. There is insufficient evidence regarding adverse cardiac dysfunction and systemic symptoms of hypothyroidism. Hence each subject's thyroid function were uniquely evaluated and the relationship between serum total T4, total T3 with free T3, free T4, TSH and anti- TPO were examined in each individuals and data's were tabulated.

Our data indicate differentiation between subclinical and overt hypothyroidism disease is somewhat arbitrary because it depends on a considerable extend on the positive of the patients normal set point for total T3, total T4, free T4, free T3, and TSH, anti TPO. We undertook longitudinal study variation of thyroid function in fifteen healthy women and our data indicate each individual add a unique thyroid function accordingly to the test result within laboratory reference limits. Data shows distinction between subclinical and overt thyroid disease is somewhat arbitrary. About 10% women have an elevated level of TPO antibody made for screening women with TPO antibody positive cases, who are at risk of developing thyroid dysfunction.

CONCLUSION

In conclusion, it was that found reference range for serum total T3, Total T4, free T3, free T4, TSH, and anti- TPO for the individuals who are living around S.R.M. Medical College, Kattankulathur and mean value was taken. We found that in some individuals who were supposed to be normal in clinical condition also had the abnormal values in thyroid function. Serum TSH value outside the population bound reference range indicates there is a possibility of a subclinical hypothyroidism. When we have some patients with false positive tests and they are having abnormal TSH then this abnormal TSH value may revert to normal value over time. The early identification of subclinical hypothyroidism on screening and early treatment prevents the progression of thyroid dysfunction. Hence, a result within the laboratory reference limit is not necessarily normal for the individuals. Another potential harm is to treat the healthy patients based on false positive test result. An elevated TSH level is a risk factor for the later development of overt hypothyroidism

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Table 1: Different levels in control group

Sr. No.	TSH (µIU/ml)	Total-T3 (ng/ml)	Total-T4 (ng/ml)	Free-T3 (pg/ml)	Free-T4 (ng/dl)	Anti-TPO (IU/ml)
1	2.50	1.20	90.30	2.80	1.34	66.00
2	4.50	1.30	92.56	2.60	1.84	62.00
3	2.80	1.76	111.67	1.90	1.39	61.48
4	4.31	1.77	116.35	3.10	1.42	40.00
5	4.60	1.47	124.79	3.40	1.68	35.00
6	2.30	1.78	135.00	2.90	1.85	36.90
7	2.11	1.64	128.75	2.70	1.50	47.50
8	2.20	1.56	118.13	1.98	1.30	37.00
9	2.22	1.28	92.30	2.82	1.28	50.00
10	4.20	1.30	123.75	2.68	1.32	36.00
11	2.90	1.72	133.75	2.23	1.42	37.00
12	2.20	1.28	142.50	1.50	1.62	62.00
13	2.30	1.42	152.80	1.69	1.78	56.00
14	2.26	1.30	130.80	2.32	1.38	64.00
15	2.24	1.98	148.60	2.48	1.42	54.00
Mean	2.90	1.51	122.80	2.47	1.50	49.65
± SD	0.96	0.24	19.66	0.53	0.19	11.82

Table 2 : **Different levels in test group**.

Sr. No.	TSH (µIU/ml)	Total-T3 (ng/ml)	Total-T4 (ng/ml)	Free-T3 (pg/ml)	Free-T4 (ng/dl)	Anti-TPO (IU/ml)
1	15.00	0.97	84.00	1.99	0.91	78.00
2	24.00	0.68	78.00	0.60	0.92	75.00
3	13.59	0.76	155.00	1.89	1.20	103.4
4	10.80	0.99	145.00	1.07	1.90	91.00
5	22.00	0.89	58.00	1.77	1.12	88.00
6	15.00	1.02	155.00	1.80	0.92	121.00
7	15.00	0.97	180.00	0.40	0.80	80.00
8	13.50	0.55	150.00	1.33	0.96	94.00
9	15.00	0.83	170.00	0.32	0.78	87.00
10	14.30	0.42	80.00	0.87	0.82	102.70
11	15.00	0.62	90.00	2.05	1.20	85.20
121	13.13	0.58	75.00	1.82	1.10	138.70
13	15.00	0.92	70.00	1.02	1.42	126.20
14	15.00	0.79	127.41	1.72	0.82	106.70
15	15.00	0.82	130.00	0.92	0.90	147.20
Mean	15.42	0.78	116.49	1.30	1.05	101.60
± SD	3.30	0.18	41.38	0.59	0.29	22.41
P- value	0.05	0.05	Not significant	0.05	Not significant	0.05

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