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ORIGINAL RESEARCH

To Study The Human Adropin Levels In Patients With Subclinical Hypothyroidism

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ABSTRACT

Introduction: The prevalence of hypothyroidism is (1-2%) of all the thyroid disorders in the worldwide. In Indian populations, average prevalence of subclinical hypothyroidism (10.8%) in adult. Subclinical hypothyroidism (SCH) it is an early stage of hypothyroidism to indicate mild thyroid gland failure. In which normal levels of triiodothyronine (T3), thyroxine (T4) and elevated levels of thyroid stimulating hormone (TSH). Adropin is a unique hormone protein composed of 43 amino acids residues and it is produced from 76 amino acid precursors. This study plan to determine the levels of adropin in patients with subclinical hypothyroidism. **Materials and methods:** The present study was done at byramjee jeejeebhoy government medical college and sassoon general hospital, pune. Clinically diagnosed subclinical hypothyroid 100 samples and normal healthy controls 100 samples with age and sex matched. **Results and discussions:** Thyroid stimulating hormone (TSH) was found significantly elevated in subclinical hypothyroid patients when compared to controls ($p < 0.0001$*). However, other thyroid parameters triiodothyronine (T3), thyroxine (T4) did not show any significant differences between the two groups. The adropin levels was significantly lower in the subclinical hypothyroid when compared to controls ($p < 0.0001$*). The elevated levels of thyroid stimulating hormone and reduced levels of adropin are associated with metabolic disorders including one of the major risk factor may occurs such as cardiovascular disease. **Conclusion :-** According to the present study results, increased levels of thyroid stimulating hormone and decreased levels of adropin in subclinical hypothyroid patients are compared to healthy controls.

Keywords: Subclinical hypothyroidism, Thyroid stimulating hormone, Adropin.

INTRODUCTION

Thyroid dysfunction is one of the most prevalent condition which occurs through endocrinopathies across the globe.[1] The prevalence of spontaneous hypothyroidism is (1-2%) around of all thyroid disorders in the worldwide.[2] In Indian population, prevalence of subclinical hypothyroidism (SCH) is (10.8%) in adult.[3] Thyroid disorders are the second most common glandular disorders of the endocrine system.[4] In which hypothyroidism represents is the most common thyroid gland disorders in worldwide and it has characterised by decreased levels of thyroid hormone that results in iodine deficiency / thyroid gland destruction by autoimmunity / surgery / radiation.[5]

The terms of subclinical hypothyroidism (SCH) it is an early stage of hypothyroidism called 'Mild Thyroid Gland Failure'. In which the measurement of thyroid stimulating hormone (TSH) levels considered to be the best screening test for thyroid disease; elevated levels usually indicates that hypothyroidism and depleted levels usually indicates that hyperthyroidism.[6] This state an elevated levels of thyroid stimulating hormone (TSH) with a normal levels of triiodothyronine (T3), thyroxine (T4) is referred to as 'Subclinical Hypothyroidism'(SCH). The terms of "Subclinical" it may since, in some of these patients may have clinical symptoms. Thyroid stimulating hormone (TSH) levels increased which reflects the sensitivity of the hypothalamic pituitary axis to decreases circulating thyroid hormones levels; as the thyroid gland failure, the (TSH) levels may be rises above the upper reference range when the free thyroxine (T4) levels has decrease or still within the normal reference range.[6]

Adropin a unique hormone was identified in (2008) which is expressed mainly in the brain, liver and heart.[7,8] Adropin peptide protein composed of 43

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amino acids residues and it has produced from the proteolytic cleavage of 76 amino acid precursors.[7] Adropin carries important functions in cardiovascular disease.[9] Adropin levels increased are associated with increased levels of nitric oxide (NOx) to reduced arterial stiffness. Thus, it possible that reduced levels of adropin may promote to arterial stiffness via NO - dependent signaling and potentially adropin protein acts as a anti-inflammatory marker.[10,11] Overall, these results suggest that decreased levels of adropin may promote arterial stiffness to exert direct effects on the endothelium systems.[9,11]

Inadequate of serum thyroid hormone produces to impairment of cardiac functions and may results in bradycardia, endothelial dysfunctions, increased intima-media thickness, diastolic dysfunction, increased vascular resistance and pericardial effusion.[12] The reduced levels of adropin protein are associated with metabolic disorders including one of the major risk factor cardiovascular disease may occurs.[13,14] This line of inquiry would position of this novel adropin protein as a potential gatekeeper of vascular systems health and may consequently implicate it as an important component of cardio - metabolic diseases.[11]

There is no any comparative data are available regarding quantitations of adropin levels among human subclinical hypothyroid patients.

The present study aimed to determine the levels of adropin in subclinical hypothyroid patients.

MATERIALS AND METHODS

Study design :- The present research study design under the analytical study of observational case-control study.

Types of study :- A case-control study.

Study Setting :- The study was done at byramjee jeejeebhoy government medical college and sassoon general hospital, pune (B.J.G.M.C & SGH, Pune) were patients are attending general medicine department. [Outpatient department (OPD)].

Diagnosed with subclinical hypothyroidism (SCH) clinically were included in the present study.

Selection and Distribution of Study Subjects

- Normal healthy controls - 100 samples were selected ; based on thyroid profile test with normal levels of (T3, T4 & TSH).
- Subclinical hypothyroidism - 100 samples were selected ; based on thyroid profile test with normal levels of (T3), (T4) and elevated levels of (TSH)
- With age and sex matched controls were selected (Ratio 1:1). **(Table No.01).**

Table 1: Distribution of healthy controls and subclinical hypothyroid.

Study Groups	Age Group	Number of subjects
Healthy Control	18-75 Years	100
Subclinical Hypothyroidism (SCH)	18-75 Years	100

Inclusion criteria :- The study subjects of subclinical hypothyroid patients having (T3), (T4) are within normal reference range and elevated levels of (TSH) and the healthy controls having (T3), (T4) and (TSH) levels are within normal reference range with age group (18-75) years both genders were included in the present study.

Exclusion criteria :- Patients having any history of external radiation, previous radioactive iodine therapy, patients with diabetes mellitus, cardiovascular disease, smokers and other systemic illness and patients on statins were excluded from the study.

Blood sample collection :- Venous blood samples were drawn approximate 5.0ml in a 12 hrs fasting in plain bulb from the patient of clinically diagnosed subclinical hypothyroidism patients with all aseptic precautions. Blood samples were centrifuged within 30 min. at 3000 rpm for 5 min and serum sample was separated and use for the estimations.

Methods of estimations

- Thyroid hormone profile test (T3, T4 and TSH) was estimated by electrochemiluminescent immunoassay method.[15,16,17]
- Adropin was estimated by enzyme linked immunosorbent assay (ELISA) kit method.[18]

Statistical analysis

Statistical analysis was done by using student ‘t’ test and data was entered in MS excel and expressed as mean and standard deviation (SD). Probability values of ($p < 0.05$) were considered to be statistically significant value.

RESULTS

In present study the mean age of patients (39.92 ± 14.00) years (mean ± SD) in subclinical hypothyroid cases while it was compared to healthy controls (36.38 ± 11.48) years (mean ± SD) ($p < 0.0520$) with age group of (18–75) years, gender / sex matched with both study group subjects. In subclinical hypothyroid group, the present study revealing that the significant differences were found primarily in the thyroid profile parameters in which the thyroid stimulating hormone (TSH). The mean TSH levels in subclinical hypothyroid group was markedly elevated at (17.3162 ± 18.5770 µIU/ml), when compared to healthy controls group (2.0283 ± 1.0131 µIU/ml), with these difference being highly statistically significant ($p < 0.0001$*).

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However, other thyroid profile parameters, including triiodothyronine (T3), thyroxine (T4), did not show any significant differences between the two groups. The mean (T3) levels (1.2241 ± 0.3319 ng/ml) in the subclinical hypothyroid group when compared to healthy controls group (1.2291 ± 0.2840 ng/ml) ($p < 0.9090$) and (T4) levels (8.7222 ± 2.2908 pmol/l) in the subclinical hypothyroid group when compared to healthy controls group (8.9823 ± 2.5563 pmol/l) ($p < 0.4495$).

The mean adropin levels was significantly lower in the subclinical hypothyroid group, with a mean of (408.828 ± 101.180 pg/ml) when compared to healthy controls group (507.732 ± 125.962 pg/ml) ($p < 0.0001$) **(Table No. 2)**.

Table 2: Age, Sex, Thyroid Profile and Adropin in patients with subclinical hypothyroidism as compared with healthy controls.

Parameters	Healthy Controls Mean ± SD	Subclinical Hypothyroidism Mean ± SD	p value
Age (years)	36.38 ± 11.48	39.92 ± 14.00	< 0.0520
Sex (Male, Female)	Female :- 90 Male :-10	Female :- 90 Male :- 10	--
T3 (ng/ml)	1.2291 ± 0.2840	1.2241 ± 0.3319	< 0.9090
T4 (pmol/l)	8.9823 ± 2.5563	8.7222 ± 2.2908	< 0.4495
TSH (µIU/ml)	2.0283 ± 1.0131	17.3162 ± 18.5770	< 0.0001*
Adropin (pg/ml)	507.732 ± 125.962	408.828 ± 101.180	< 0.0001*

* Values expressed in Mean ± SD

* $p < 0.05$ = Significant, $p < 0.001$ = Highly Significant, $p > 0.05$ = Non Significant (N.S.)

DISCUSSION

In present study shown the significantly elevated thyroid stimulating hormone (TSH) levels in subclinical hypothyroidism as compared with healthy controls. Thyroid stimulating hormone (TSH) levels increased to reflects the sensitivity of hypothalamic pituitary axis to decreases the levels of thyroid hormones in a circulating systems; as a results of thyroid gland failure to observed that thyroid stimulating hormone (TSH) levels may rises above the upper reference range when thyroxine (T4) levels within the normal range.[6] Other several causes of subclinical hypothyroidism such as, autoimmune thyroiditis (hashimoto's thyroiditis), iodine deficiency, medication, radiation therapy and genetic factors.[19] And the complications of subclinical hypothyroidism like cardiovascular disease, lipid dysfunctions, mood and cognitive changes.[20]

Subclinical hypothyroidism in worldwide may be the higher risk for the progression of overt hypothyroidism are primarily affecting by older adults with abnormal thyroid stimulating hormone (TSH) levels may be a novel of cardiovascular risk factor. Previous large scale study (meta – analyses) have evaluate the major risks factors of cardiovascular disease with subclinical hypothyroidism. Another study (meta - analysis) of cardiovascular mortality was higher in patients with age group < 65 years old with subclinical hypothyroidism.[20]

The reduced levels of adropin are related with major risk factors for coronary vascular disease.[13] Celik A et al. A patients with cardiac syndrome X (CSX) was found that the low levels of circulating adropin, suggesting that low levels of adropin are risk factors for cardiac syndrome X (CSX).[14] Yu et al. was found that reduced levels of adropin in a patients with coronary artery disease predicts the incidence of acute myocardial infarction.[21] Thus, down-regulation of adropin levels may promote or contribute to impairment of energy homeostasis in a disease state.[22] No comparative data are available regarding quantitations of adropin levels among human subclinical hypothyroid patients.

CONCLUSION

According to the present study results, increased levels of thyroid stimulating hormone (TSH) and decreased levels of adropin in subclinical hypothyroid patients are compared to healthy controls.

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