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Original Research Article

Prospective Study Establishing Relationship between Hypertension And Subclinical Hypothyroidism

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ABSTRACT

Background: Dyslipidaemia and arterial hypertension are risk factors for atherosclerosis. The idea that overt hypothyroidism promotes atherosclerosis has been generally accepted, but whether sub-clinical hypothyroid (SCH) is associated with increased risk of atherosclerosis, is still a matter of debate. Hence; we planned the present study to evaluate sub-clinical hypothyroid (SCH) effects on blood pressure and lipids.

Materials & Methods: The present study included assessment of effect of SCH on blood pressure and lipid profile. Prospective analysis of a total of 15 patients was done, out of which 12 were females and 3 were males. Another ten individuals who were healthy and euthyoid, were taken as controls in the present study. Complete physical examination of all the subjects was done along with their complete biochemical analysis. Patients were called in the morning and blood samples were withdrawn and were sent to central laboratory for further analysis. All the results were analysed by SPSS software.

Results: Non- significant results were obtained while comparing the mean FT4 values in between the study group and control group. Highly significant results were obtained while comparing the mean TSH in between the study group and the control group. Total cholesterol levels of more than 53.2 mmol/l was seen in 8 subjects of study group and 5 subejcts of control gorup respectively.

Conclusion: Arterial hypertension and dyslipidaemia do occur in significant proportion in SCH subjects.

Key words: Hypertension, Lipid, Subclinical Hypothyroidism.

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INTRODUCTION

Thyroid gland along with the parathyroid glands and heart share a close relationship arising in embryology. In ontogeny, the thyroid and heart migrate together. There is a strong physiological relationship between the two organs, which is affirmed by predictable changes in cardiovascular functions across the entire range of thyroid disease states.[1-3] Many symptoms and signs recognized in patients with overt hyperthyroidism and hypothyroidism are due to increased or reduced action of thyroid hormone on the heart and the vascular system, respectively.[4]

Increases in parathyroid hormone (PTH) have been associated with changes in the vascular tone and renin angiotensin system. Hyperfunctioning parathyroid glandular disorders have been for long associated with an increased risk of hypertension, though a causal relationship is still not established.[5-7]

Dyslipidaemia and arterial hypertension are risk factors for atherosclerosis. The idea that overt hypothyroidism promotes atherosclerosis has been generally accepted, but whether SCH is associated with increased risk of atherosclerosis, is still a matter of debate.[8-10] Hence; we planned the present study to evaluate sub-clinical hypothyroid (SCH) effects on blood pressure and lipids.

MATERIALS & METHODS

The present study was conducted in the Department of General Medicine, Sri Lakshmi Narayana Institute of Medical Sciences, Osudu, Puducherry (India) and included assessment of effect of SCH on blood pressure and lipid profile. Ethical approval was taken from institutional ethical committee and written consent was obtained from all the subjects after explaining in detail the entire research protocol. Prospective analysis of a total of 15 patients was done, out of which 12 were females and 3 were males. New cases of SCH were defined as follows:

- Normal free thyroxine (fT4) levels in between 10.3 to 24.45 pmol/l,
- Elevated thyrotropin (TSH); more than 4.2 mU/l.

Another ten individuals who were healthy and euthyoid, were taken as controls in the present study. The mean age of the subjects in the present study was 42.25 years, while mean BMI

was found to be 29.24 Kg/m^2. Mean age of the subjects of the control group was 48.22 years while mean BMI of the subjects of the control group was 28.41 Kg/m^2.

Exclusion Criteria

- Patients with history of any other systemic illness,
- Patients with any known drug allergy,
- Patients with previous history of thyroid disease,
- Patients who took any medication related to thyroid disease,
- Patients who took any medication related to lipid metabolism.

Complete physical examination of all the subjects was done along with their complete biochemical analysis. Patients were called in the morning and blood samples were withdrawn and were sent to central laboratory for further analysis. Complete haematological and endocrinological picture of all the patients was obtained and was assessed. All the results were analysed by SPSS software. Chi- square test and one way ANOVA were used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

RESULTS

Demographic and personal details of all the subjects of SCH group and control group is shown in Table 1. FT4 value in between in SCH group and the control group was found to be 15.24 and 17.44 respectively. Non- significant results were obtained while comparing the mean FT4 values in between the study group and control group (p- value < 0.05).

Mean TSH value in the study group and the control gorup was found to be 9.11 and 160.34 respectively (Graph 1). Highly significant results were obtained while comparing the mean TSH in between the study group and the control group (p- value < 0.05).

Table 2 shows the lipid profile of subjects of both the study groups. Total lipids content of more than or equal 10 gm/l was seen in 5 subjects of the study group and 3 subjects of the control group respectively. Total cholesterol levels of more than 53.2 mmol/l was seen in 8 subjects of study group and 5 subjects of control gorup respectively.

Table 1: Demographic and personal details of the subjects

Parameter		SCH (N= 15)	Control (N= 10)	p- value
Gender	**Male**	3	2	0.25
	Female	12	8	
Mean age (years)		42.25	48.22	0.15
Mean BMI (Kg/m^2)		29.24	28.41	0.31
FT4 (pmol/l)		15.24	17.44	0.98
TSH (mU/l)		9.11	160.34	0.01*

*Significant

Graph 1: Descriptive values for hormonal details of the subjects of both the study gorups

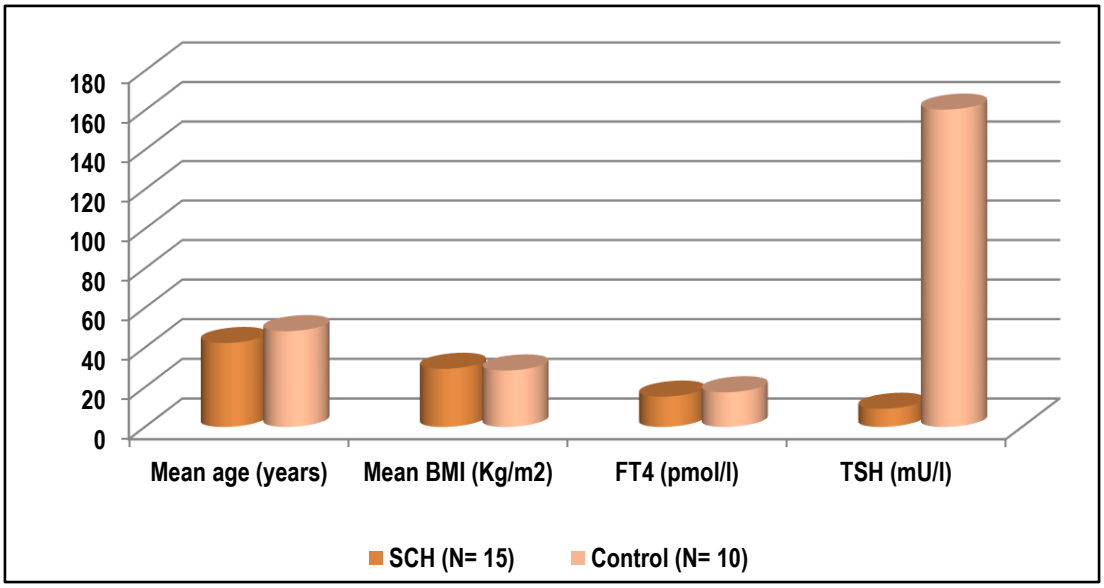

Table 2: Lipid profile of subjects of both the study groups

Parameter	SCH (N)	Control gorup (N)
Total lipids (≥ 10 g/l)	5	3
Triglycerides (≥ 2 mmol/l)	6	2
Total cholesterol (> 5.2 mmol/l)	8	5
Arterial Hypertension (≥ 140/90mmHg)	4	1

DISCUSSION

In the present study, we observed that arterial hypertension was present in approximately forty percent of the subjects with SCH (Table 2). Park CW et al determined the effect of thyroxine therapy on renin-angiotensin-aldosterone system (RAAS) and neurohormones affecting water and electrolyte metabolism and the reason for these changes in patients with primary myxoedema. They measured changes in the plasma renin activity (PRA), serum aldosterone (Aldo), antidiuretic hormone (ADH), atrial natriuretic hormone (ANH) levels, serum and 24 h urinary electrolytes and osmolalities, and cardiac function in 22 female patients with primary myxoedema before and after correction of hypothyroidism. We also evaluated age-, sex-, and BMI-matched 15 healthy control subjects. It took an average of 4.3 months (range, 3-9 months) to normalize thyroid function. The mean reductions of body weight and estimated plasma volume were 1.8+/-1.0 kg (P=0.002) and 8.5% (P<0.001), respectively. In addition, serum Na+ and osmolality and the haematocrit were significantly elevated after correction of hypothyroidism (P<0.01 and P<0.001, respectively). Increased F(E)Na and C(OSM) (P<0.05) levels in patients with hypothyroidism (Ho) compared with those in Cont did not change after thyroxine therapy (Eu). However, C(H(2)O), U(E)K, F(E)K, and TTKG levels as well as creatinine clearance (Ccr) were markedly increased in Eu compared with Ho and Cont (P<0.01, respectively). Increased plasma ADH concentration and decreased plasma ANH concentration were normalized compared to Cont after thyroxine therapy (P<0.001 and P<0.01, respectively). Low PRA and serum Aldo concentration in Ho were significantly increased in Eu (P<0.001 and P<0.01, respectively). In addition, increased left ventricular mass index and decreased cardiac output in Ho were normalized compared to Cont after thyroxine therapy (P<0.01, respectively) These findings suggested that the exaggerated upregulation of RAAS after correction of hypothyroidism in patients with primary myxoedema is associated with an increase in Ccr and a decrease in plasma volume resulting from water diuresis, natriuresis, osmotic diuresis and inappropriate changes in plasma ADH and ANH levels. The improved renal function coincided with an amelioration of cardiac function. These changes seem to be an adaptive response for preventing excessive plasma volume and weight loss after thyroxine therapy.[11]

Biondi B et al investigated the endothelial response of coronary flow in young and middle-aged patients with SHypo, without associated cardiovascular risk factors compared with healthy control subjects. The study population consisted of 20 women (mean age 38.4+12.1 years) with newly diagnosed, untreated and persistent SHypo due to Hashimoto's thyroiditis. A total of 15 volunteers served as controls. Age, gender, body surface area, glucose, insulin levels, heart rate, systolic, diastolic, and mean blood pressure were similar in patients and controls. Body mass index was significantly higher in SHypo patients. Total cholesterol and low-density lipoprotein cholesterol, despite not significant, tended to be higher, and high-density lipoprotein cholesterol to be lower in SHypo. Coronary blood flow velocities were recorded in patients at rest and after the cold pressor test (CPT), a stimulus that can be considered totally endothelium-dependent. CFR was calculated as the ratio of hyperemic-to-resting diastolic peak velocities. Coronary diastolic peak velocities at rest did not differ between the two groups but were significantly lower after CPT in patients with SHypo, thereby resulting in a lower CFR. The difference remained significant after adjusting resting and CPT velocities for the respective mean blood pressures. TSH was inversely correlated with CFR in the pooled population. Patients with SHypo without associated cardiovascular risk factors have a coronary endothelial dysfunction that appears in response to a physiological stimulus (the CPT).[12]

Rosário PW et al evaluated the natural history of this milder form of SCH (TSH < or =10 mIU/L with normal thyroid hormone levels) in adult women patients. One hundred seventeen patients with TSH levels ranging from 5 to 10 mIU/L and normal free T4, without a previously known history of thyroid disease, were followed for a period of 3 years and had two consecutive assessments. Sixty patients tested positive for antithyroperoxidase antibodies (TPOAb) and 36 were TPOAb negative but had diffuse hypoechogenicity on thyroid ultrasound (US). Twenty-one patients were TPOAb negative and had normal US. During follow-up, 20.5% of the patients had spontaneous normalization of their TSH, 27.3% required replacement therapy with levothyroxine (L-T4) because of progression to overt hypothyroidism or persistence of serum TSH >10 mIU/L, and 52.1% continued to meet the criteria for mild SCH (persistence of TSH < or =10 mIU/L). If the patients were classified into two groups, one with positive TPOAb and/or US alteration and the other with testing negative for TPOAb and not having US alteration, the first group had a greater progression toward overt hypothyroidism (31.2% vs. 9.5%, respectively) and a lower rate of normalization of TSH (15.6% vs. 43% respectively). These rates were similar in TPOAb-positive patients and patients with negative TPOAb but with positive US. Most patients with SCH and TSH < or = 10 mIU/L do not progress to overt hypothyroidism. The presence of chronic thyroiditis as demonstrated by US increases the evolution of SH to overt hypothyroidism or more severe SCH and thus the need for L-T4 treatment. US findings are important in determining the prognosis of mild SCH.[13]

CONCLUSION

From the above results, it can be concluded that arterial hypertension and dyslipidaemia do occur in significant proportion in SCH subjects. However, future studies are recommended.

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