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RESEARCH ARTICLE

A STUDY OF CORRELATION BETWEEN THYROTROPIN AND BODY MASS INDEX IN EUTHYROID SUBJECTS

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ABSTRACT

Objective: To investigate the relationship between circulating Thyroid Stimulating Hormone level and adiposity in a cohort of people having normal thyroid function.

Methods: Retrospective cross-sectional analysis was carried out on 104 Euthyroid female patients. Forty Euthyroid females with (BMI <23 kg/m^2) and Sixty four Euthyroid females with (BMI >23 kg/m^2 subjects were included in the study group. TSH, Thyroxine (T4), Triiodothyronine (T3), fasting glucose, Total cholesterol, Triglyceride, High Density lipoprotein-Cholesterol, body weight, height and Body Mass Index (BMI) were assessed.

Results: Serum TSH levels were higher in the obese than in the lean Euthyroid subjects. In the study group II, there was a significant positive correlation between serum TSH and body weight (r = 0.43, p =0.0003), BMI (r = 0.53, p=0.0001).There was also positive correlation between serum TSH and Total Cholesterol, Triglyceride but statistically not significant.

Conclusions: This study strongly supports evidence that serum TSH levels are positively correlated with the degree of obesity and some of its metabolic consequences in overweight people with normal thyroid function.

INTRODUCTION

Thyroid stimulating hormone (TSH) an eminent endocrine pituitary hormone, its action is to regulate the function of the thyroid gland. The serum level of thyrotropin is a reliable index of the biological activity of thyroid hormones. As a prime regulator of energy balance, the contribution of thyroid hormones to the maintenance of body weight has been the subject of numerous clinical studies (Rosenbaum *et al.,* 2000). Lipid and thyroid profiles are the most common investigations asked for in patients having weight gain by clinicians. Therefore measurement of serum levels of TSH has been a consistent component of the clinical studies on the relationship between thyroid function and adiposity (Roti *et al.,* 2000, Ritz *et al*., 2002). The conclusion from some of these studies has been that weight gain increases serum levels of TSH; yet, others showed no relationship between TSH

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and body weight (Krotkiewski *et al.,* 2000). Although data linking weight change with thyroid functions has been studied by many researchers there is only few studies in normal thyroid function subjects, Evidence emerging that thyrotropin induces adipogenesis and adipokine production directly, independent of the mediating influence of thyroid hormones on energy balance (Tagliaferri *et al.,* 2001), prompted us to reinvestigate the relationship between circulating TSH levels, body weight and the metabolic consequences of adiposity in a cohort of Euthyroid people, with normal thyroid function. (Zimmermam-Belsing *et al.,* 2003).

MATERIALS AND METHODS

Retrospective cross-sectional analysis was carried out on 104 Euthyroid patients referred for their thyroid profile to the Department of Biochemistry, Vinayaka Missions Medical College and Hospital were selected for the study. Any of the following reasons: male gender, history of thyroid disease, abnormal thyroid hormone levels, history of radioiodine treatment, being on treatment with thyroid hormone, antithyroid drugs or any drug that might affect evaluation of thyroid status were excluded from the study. A brief clinical history, systemic examination was done and informed consent was taken from the study subjects.

Anthropometrical measurements

Body weight (kg) and height (m) were measured and BMI was calculated as weight divided by squared height (kg/m^2).

Biochemical parameters

Fasting blood specimen obtained from the study subjects were centrifuged for serum separation and used for the following biochemical assays

Estimation of Serum TSH*:* EIA Kit obtained from Ranbaxy Laboratories was used. In a quantitative Enzyme Immuno Assay (EIA) (Hopton MR *et al.,* 1986, Demers *et al.,* 2007), high affinity antibodies react with antigen to form an insoluble sandwich complex on the surface of a coated micro plate. The antigen from the specimen gets linked at the surface of the well through interaction of reactive IgG coated on the well and affinity purified x-antigen IgG conjugated with Horse Radish Peroxidase (HRP). The fraction of the x-antigen IgG conjugated with enzyme that does not bind to the coated well is washed away. The enzyme activity, which is proportional to antigen concentration in the sample, is measured by addition of substrate. By utilizing calibrators of known antigen values, a dose response curve can be generated from which the antigen concentration in a sample can be found out by reading the absorbance in each well at 450nm (using a reference wavelength of 620-630nm to minimize well imperfection) in ELISA reader.

Estimation of Serum Total Thyroxine (T_4): EIA Kit obtained from Ranbaxy Laboratories was used (Sterling *et al.,* 1975). In a competitive EIA, enzyme linked antigen competes with antigen from the specimen for a limited number of binding sites on the immobilized antibody coated on the micro wells. Unbound antigen fraction is then washed away. The enzyme activity in the antibody bound function which is inversely proportional to the native antigen concentration is measured by addition of the substrate. By utilizing calibrators of known antigen values, a dose response curve may be generated from which the antigen concentration of an unknown can be obtained by reading the absorbance in each well at 450nm (using a reference wavelength of 620-630nm to minimize well imperfection) in ELISA reader.

Estimation of Serum Total T_3: EIA Kit obtained from Ranbaxy Laboratories was used (Sterling *et al.,* 1975). In a competitive EIA, enzyme linked antigen competes with antigen from the serum for a limited number of binding sites on the immobilized antibody coated on the micro wells. Unbound antigen fraction is then washed away. The enzyme activity in the antibody bound function which is inversely proportional to the native antigen concentration is measured by addition of the substrate. By utilizing calibrators of known antigen values, a dose response curve may be generated from which the antigen concentration of an unknown can be obtained by reading the absorbance in each well at 450nm (using a

reference wavelength of 620-630nm to minimize well imperfection) in ELISA reader.

Estimation of Serum Cholesterol: CHOD – POD Enzymatic colorimetric end point Method. Cholesterol esters are hydrolysed to produce cholesterol. Hydrogen peroxide is then produced from oxidation of cholesterol by cholesterol oxidase. The indicator quinoeimine is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxide. The absorption of the red quinoneimine dye is proportional to the concentration of cholesterol in the sample at 505nm.

Estimation of Serum Triglycerides: - GPO – PAP enzymatic colorimetric end point Method (Buccolo, 1973). Triglycerides are determined after enzymetic hydrolysis with lipases. The quinonemine indicator is foamed from hydrogen peroxide, aminophenazone and 4-chlorophenol under the catalytic influence of peroxidise. Then measure absorbance of sample (AT) and standard (AS) against reagent blank at 505nm in the semi auto analyzer.

Estimation of serum HDL-Cholesterol: Precipitating reagent end point Method (Denahcherp, 1980). Low density lipoproteins (LDL and VLDL) and chylomicron fractions are precipitated by the precipitating reagent. After centrifugation, the cholesterol concentration in the HDL (high density lipoproteins) fraction remains in the supernatant in this phase and is determined by an enzymatic CHOD-PAP method.

Estimation of blood glucose: Enzymatic colorimetric end point GOD-POD method (Trinder, 1970). Glucose is determined after enzymatic oxidation in the presence of glucose oxidase. The hydrogen peroxide formed reacts, under catalysis of peroxidases.With phenol and 4-aminophenazone to form a red-violet quinoeimine dye as indicator and measure absorbance of sample (AT) and standard (AS) against reagent blank at 505nm in the semi auto analyzer.

Statistical analyses

All statistical analyses were performed using SPSS 9.0 software. Data are presented as Means±SD. Correlation between measured parameters was assessed using the analytical method of partial correlation and coefficient of correlation.

RESULT

104 Euthyroids selected based on their serum TSH in normal range between 0.4 and 6.0 uIU/mL (equivalent to mIU/L) and normal total T4 and T3 value. The study subjects were further categorised on the WHO Expert Consultation: Appropriate body mass index for Asian pacific Populations as Group I with 40 Euthyroid females having (BMI <23 kg/m^2) and Group II with 64 Euthyroid females having (BMI >23 kg/m^2). Mean TSH in GROUP II (BMI >23 kg/m^2) observed to be higher than Group I (BMI <23 kg/m^2) and found to be statistically significant (Table 1).

Table 1. Antropometric and biochemical parameters in study subjects

Parameter	GROUP I MEAN ± SD	GROUP II MEAN ± SD
AGE (years)	36.8 ± 8.84	35.4 ± 8.9
BODY WEIGHT (Kg)	52.4 ± 10.2	61.2 ± 18.4
BMI (kg/m^2)	21.1 ±0.8	25.7 ± 2.5
TSH (mIU/L)	1.97 ± 0.8	3.7 ± 1.1*
Total T4(µg/dl)	7.29 ± 2.06	8.05 ± 2.4
Total T3(ng/ml)	1.2 ± 0.76	0.99 ± 0.4
Fasting GLUCOSE (mg/dl)	95.7 ± 16.8	96.4 ± 23.47
Total CHOLESTEROL (mg/dl)	173.5 ± 23.7	177.1 ± 19.9
TRIGLYCERIDE (mg/dl)	142.5 ± 35.1	143.8 ± 30.4
HDL-CHOLESTEROL (mg/dl)	44.4 ± 3.36	48.04 ± 6.8

Table 2. Correlation of TSH with anthropometric and lipid parameters in the study groups

Parameter	Group I r- value	Group II r- value
BODY WEIGHT(Kg)	0.26	0.43*
BMI (kg/m^2)	0.31*	0.53*
Total.CHOLESTEROL (mg/dl)	0.05	0.19
TRIGLYCERIDE (mg/dl)	0.09	0.13
HDL-CHOLESTEROL (mg/dl)	0.08	0.12

(* statistically significant p-value)

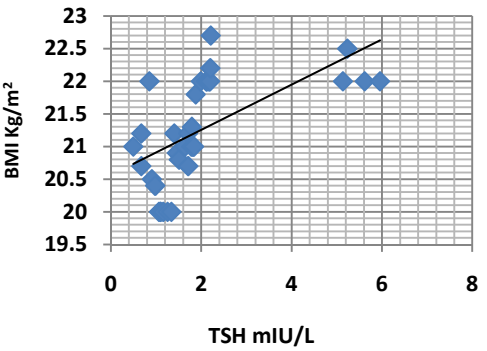

Fig.1.Correlation of TSH VS. BMI in group I (BMI <23 Kg/m^2)

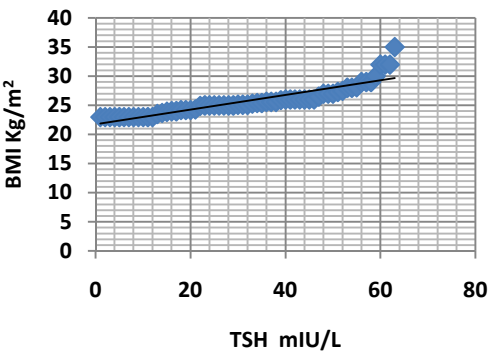

Fig. 2. Correlation of TSH vs BMI in group II (BMI >23 kg/m^2)

Total cholesterol in Group II (177.1 ± 19.9 mg/dl) is in increased level compared to Group II (173.5± 23.7 mg/dl). Also serum Triglyceride and HDL-Cholesterol was observed to be in increased level in Group II but statistically not significant. All the lipid parameters were observed to be in normal range in both the study Groups. The correlation of serum TSH with body weight and BMI was observed to be positively associated in both the Euthyroid study subjects and statistically more significant in Group II (BMI >23 kg/m2) than compared to Group I (BMI <23 kg/m2). Serum Total cholesterol, Triglyceride and HDL-cholesterol also observed to be positively correlated with serum TSH level but not statistically significant (Table 2).

DISCUSSION

Body mass index (BMI) or Quetelet index has been used by the WHO as the standard for recording obesity statistics since the early 1980's and is a statistical measurement which compares a person's weight and height. The formulas universally used in medicine produce a unit of measure of kg/m^2. Among Asian adults, a BMI value of >23.0 kg/m^2 is considered as obese, as per WHO Experts Consultation, Lancet 2001.

Greatly increase in thyroxine almost always decrease the body weight, and decrease in thyroid hormone increase the body weight, these effects don't always occur, because thyroid hormone also increases the appetite and this may counterbalance the change in metabolism. So it is clear overt hypothyroidism is associated with weight gain, while hyperthyroidism is associated with weight loss. Therefore overt thyroid dysfunction clearly influences Body Mass Index (Baron *et al.,* 1956, Hoogwerf *et al.,* 1984). But is unclear of their association in Euthyroid subjects. The European Study showed a positive correlation between BMI and serum TSH, a negative correlation between BMI and serum free T4, and no association between BMI and serum free T3. Obesity (BMI> 30 kg/m^2) and serum TSH levels were significantly associated in this cohort study. TSH levels were significantly higher, with high borderline values of BMI, as compared to the lower BMI values. (Knudsen *et al.,* 2005). Of 87 obese women without complications, severely obese (BMI> 40 kg/m^2) women had a higher serum TSH than mildly or moderately obese women (BMI< 40 kg/m^2), and TSH was positively correlated with BMI. This study showed a positive correlation between TSH levels and BMI in euthyroid subjects.(Iacobellis *et al.,* 2005).

The fifth Troms study reported similar finding where there was a positive correlation between varying degrees of obesity and varying TSH levels showed a positive correlation between normal-range serum TSH and BMI in nonsmokers and demonstrated no correlation between serum TSH and BMI in smokers.(Nymes *et al.,* 2006). Michalaki *et al.,* 2006 reported that morbidly obese subjects had higher levels of T3, free T3, T4, and TSH than did control.A recent study reported from United Kingdom and Korean (Acobellis *et al.,* 2005) failed to find a link between these two variables in euthyroid subjects. Serum TSH levels were higher in the obese than in the lean subjects. In the study group (lean and obese subjects), there was a significant positive correlation between serum TSH and body weight ($r = 0.231$, $p < 0.001$), BMI ($r = 0.270$, $p < 0.001$), waist circumference ($r = 0.219$, $p = 0.001$), fasting insulin ($r = 0.201$, $p = 0.002$) and HOMA-IR ($r = 0.201$, $p = 0.002$); there was no correlation between serum FT4 and any of the parameters. A multivariate linear regression analysis revealed that only BMI ($p = 0.012$, 95% CI = 0.01–0.08) contributed significantly to the variance of TSH. This study strongly supports existing, but contradictory evidence that serum TSH levels are positively correlated with the degree of obesity and some of its metabolic consequences in overweight people with normal thyroid function **(**Mehmet Bastemira *et al.,* 2007).

The association between normal-range thyroid function and BMI, and also BMI with T4 and T3 has been the subject of much debate continuing. But our findings suggest that thyroid function within the normal range is associated with BMI, but a definitive relationship is not clear at what cut off point level of TSH causes increase in BMI leading to obesity and further hyperlipidemia.

Conclusion

As serum TSH is observed to be increasing with Body mass index even in Euthyroid subjects, our results provide circumstantial evidence that the pituitary gland, via thyrotropin may indeed contribute to the evolution of obesity, independent of any involvement of the thyroid gland.

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