

Subclinical Hypothyroidism and Central Adiposity

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ABSTRACT:

BACKGROUND:

The pandemic of central obesity has driven new interest in the relationship between thyroid hormone and body weight distribution since it is well known that thyroid hormones play a key role in regulating energy homeostasis and that subtle elevation in TSH as in subclinical hypothyroidism (SCH) is associated with deficiency in resting energy expenditure and increased body weight.

OBJECTIVE:

The aim of our study was to assess possible associations of subclinical hypothyroidism with central obesity in apparently healthy women.

METHODS:

133 apparently healthy, clinically euthyrotic women were included in this study; 91 of them were centrally obese and 42 were centrally non obese, Thyroid function tests and waist circumference measurement were done in all participants.

RESULTS:

13.5 % (n=18) of the studied population had subclinical hypothyroidism. In the centrally obese group the frequency was 17.5 % (n=16), while in the non obese it was 4.7% (n=2), the highest frequency was found in the 40-49 years old women (38.8%).

Positive significant correlation was found between waist circumference and age, negative significant correlation was found between age and T₃.

CONCLUSION:

The frequency of SCH is more in centrally obese women. Assessment of thyroid function must be regarded as part of the screening program in obese.

KEYWORDS: subclinical hypothyroidism, central obesity, waist circumference.

INTRODUCTION:

Subclinical hypothyroidism (SCH) is defined as elevated thyrotropin (TSH) level with a normal free thyroxin hormone (T₄) level; the concept of subclinical hypothyroidism has emerged over the past several decades as the ability to detect subtle changes in thyroid function is progressively improved⁽¹⁾. Although it is recognized that patients with SCH may have subtle symptoms of thyroid dysfunction, the definition is purely a biochemical one⁽²⁾.

SCH has been recognized to be associated with risk of cardiac impairment and cardiovascular diseases, even minor deviation in thyrotropin normal range might accelerate the development of atherosclerosis and have adverse effect on cardiovascular performance in the general population^(3,4). SCH has also been identified as a risk for nephropathy and a strong predictor of mortality in chronic dialysis patients. Patients

with SCH have higher total cholesterol and low density lipoprotein cholesterol level than euthyroid subjects, and have increased C-reactive protein value^(5,6).

The prevalence of obesity is rising rapidly in many parts of the world. Obesity contributes to hyperglycaemia, hypertension, high serum TGs, low HDL-cholesterol and insulin resistance, and is associated with higher CVD risk and there is a striking association of obesity with Type 2 diabetes.^(7,8)

Central obesity also known as abdominal obesity is the accumulation of visceral fat or intra-abdominal fat packed between the internal organs resulting in increase in waist size⁽⁹⁾. It is associated with a higher risk of insulin resistance, syndrome and is an indicator used in the diagnosis of that syndrome. The severity of central obesity can be determined by measuring the absolute waist circumference [>102 cm (40 in) in men and >88 cm (35 in) in women]⁽¹⁰⁾ or by measuring the waist to hip ratio (>0.9 for

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men and >0.85 for women)⁽⁹⁾. Waist circumference have major advance over body mass index and provide the most clinically useful indicator of central obesity and it has now been documented that some individuals with a normal body mass index may be centrally obese, although BMI is often used in clinical settings to estimate body fat and to assess risk among adults. The use of BMI, has limitations because it has been shown that current BMI cutoffs may underestimate obesity and the associated health risk factors among populations that are not Caucasian^[11]. Furthermore, it does not account for factors such as body size and body fat distribution such as abdominal obesity. There is growing evidence to support an association between abdominal fat and CVD incidence and outcomes such as cardiometabolic risk factors^[12]. Waist circumference (WC), a simple measure of abdominal fat, has been observed to be a stronger predictor of obesity-related risk factors than BMI in older adults and that WC, and not BMI, explains obesity-related health risk^(13,14).

The obesity pandemic has driven new interest in the relationship between thyroid hormone and weight status since it is well known for decades that thyroid hormones play a key role in regulating energy homeostasis and the deep transformation in energy balance may be one of the underlying mechanisms of obesity⁽¹⁵⁾.

The aim of our study was to investigate possible associations of subclinical hypothyroidism with central obesity in apparently healthy women.

SUBJECTS AND METHODS:

This study was carried out in the period between April 2011 to October 2011, 150 apparently healthy female with age range 20 – 65 years, mean (40±5) were enrolled in this study, the participants were relative of patients attending Baghdad teaching hospital, participants were clinically euthyroidic, and without history of thyroid disease or any chronic illness or taking any medications that might affect the tested parameters, all participants underwent examination for the presence of goiter.

Definition of SCH:

SH was biochemically defined as a serum level of TSH above the normal range (0.4–4.0 mIU/l) with FT4 and T3 concentrations within the normal reference range (free thyroxine 0.82–1.63ng/dl, total T₄ 4.9–11 µg/dl, total T₃ 0.79–1.58 ng/ml)⁽²⁾.

Waist circumference were measured in a horizontal plane midway between the inferior margin of the ribs and the superior border of the iliac crest, if the waist circumference was more than 88cm (35in) the woman is considered centrally obese. Participants were divided into two groups according to their waist circumference,

Group 1; centrally obese women with waist circumference more than 88 and this group include 100 women.

Group 2; centrally non obese women with waist circumference less than 88 and this group include 50 women.

5 ml of venous blood was collected from all participants, Serum TSH, free T₄ total T₃, T₄ were done for all participants and was carried out by immunofluorometric immunoassay, TSH more than 4 IU/ml and with normal thyroid hormones level were diagnosed as subclinical hypothyroidism. Reference ranges used were: (TSH 0.4 - 4 µIU/ml, free thyroxin 0.82-1.63ng/dl, total T₄ 4.9-11 µg/dl, total T₃ 0.79-1.58 ng/ml).

After hormonal analysis 17 women were excluded as they had overt hypothyroidism or hyperthyroidism or subclinical hyperthyroidism. and the remaining 133 were distributed as:

Group 1: 91 women with increased waist circumference

Group 2: 42 women with normal waist circumference

Analysis of data was performed using statistically package for social science (SPSS) version 17.0. Results are expressed as mean ± SD. Student T test was used to compare the significance of the difference in the mean values of any two groups and chi square analysis was used to compare frequency between the two groups and P<0.05 was considered statistically significant.

RESULTS:

The anthropometric and hormonal characters of the two groups are shown in table 1. This study showed high prevalence of subclinical hypothyroidism among women in group 1 (20.5%) compared to women with normal waist circumference in group 2 (5.2%). and the prevalence in the total studied population was 15.6%.

Table 1 shows that there is statistically significance difference in waist circumference and the number of women with SCH between the two group (P=0.000)

SUBCLINICAL HYPOTHYROIDISM

Women between 40-49 years showed a greater prevalence of SCH compared to other age group. There is significant positive correlation between

waist circumference and age ($r=0.46$, $p=0.000$) as shown in figure 1. and there is negative statistically significant correlation between age and T_3 ($r=-0.27$, $p<0.05$) as shown in figure 2.

Table 1: Baseline characteristics of the studied population.

	Centrally obese women (Mean \pm SD)	Centrally non obese Women (Mean \pm SD)	P value
Number	91	42	
Age	40 \pm 8	39 \pm 7	0.9
Waist circumference (cm)	107 \pm 12	83 \pm 5	0.000
No. of women with Subclinical hypothyroidism (%)	16 (20.5 %)	2 (5.2 %)	0.000
TSH (μ IU/ml)	4.6 \pm 1.4	2.3 \pm 0.5	0.112
Free thyroxin (ng/dl)	1.24 \pm 0.3	1.01 \pm 0.1	0.341
Total thyroxin (μ g/dl)	8 \pm 2	7.8 \pm 4	0.61
Total T_3 (ng/ml)	1.13 \pm 0.04	1.25 \pm 0.08	0.23

Table 2: Characteristic of women with subclinical hypothyroidism

	SCH in group 1 Mean \pm SD	SCH in group 2 Mean \pm SD
number	16/18 (88.8%)	2/18 (11.11%)
Age (years)	38 \pm 8	36 \pm 12
Waist circumference (cm)	108 \pm 10	87.5 \pm 0.7
TSH (μ IU/ml)	9 \pm 2	11 \pm 4

Table 3: Distribution of SCH by age

AGE (years)	Number of women with SCH	Percentage of the total SCH
20-29	3	16.6 %
30-39	5	27.7 %
40-49	7	38.8 %
50-65	3	16.6 %
total	18	100%

Total number of women with SCH= 18

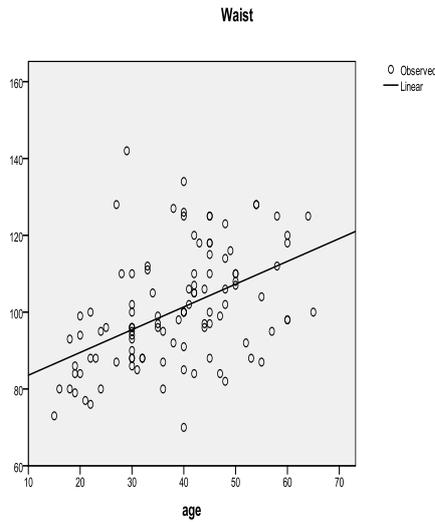


Figure 1: Positive significant correlation between WC and age ($r = 0.47, P = 0.000$)

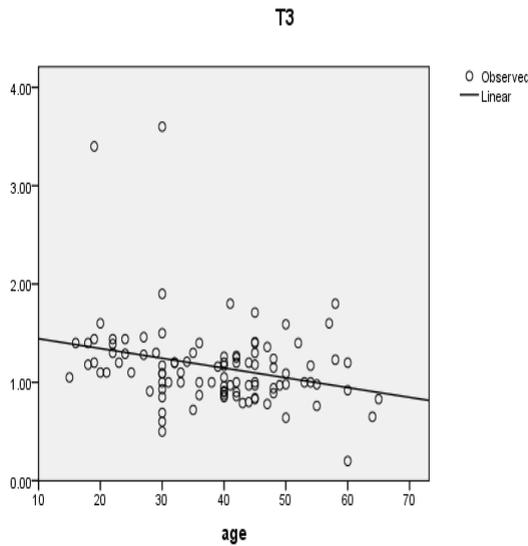


Figure 2: Shows significant negative significant correlation between age and T_3 ($r = -0.27, p = 0.006$)

DISCUSSION:

In this study the prevalence of subclinical hypothyroidism in the studied population was 15.6 % the estimated prevalence of this condition in previous study have varied from 4-15%⁽¹⁶⁾ In centrally obese women the prevalence of SCH was high 20.5% compared to 5.2% in women with normal waist circumference ($P=0.000$) ,thyroid dysfunction is associated with changes in body weight and composition, body

temperature, total and resting energy expenditure independently of physical activity, both subclinical and overt hypothyroidism is frequently associated with weight gain, decreased thermogenesis, and metabolic rate.⁽⁵⁾

The observed positive association between TSH and obesity could be due to alterations in thyroid hormones (TH) activity or as a result of an alteration in the regulation of the hypothalamic-

pituitary-thyroid (HPT) axis. The hypothesis that involves a direct effect of TSH is also plausible as the TSH receptor is expressed in adipose tissue⁽¹⁷⁾. It has been published that circulating cytokines related with metabolic syndrome can suppress thyroid function either at hypothalamic or pituitary or thyroid levels⁽¹⁸⁾.

The more suitable contributing factor is the deregulation of the Hypothalamic-pituitary-thyroid (HPT) axis in the obese population, since a direct relationship between TSH and obesity has been consistently observed⁽¹⁹⁾. However, as there are conflicting data in the literature regarding the relationship between obesity and TH. Some studies, but not all, demonstrated low T3 and low T4 at higher body weight, whereas other authors found a direct relationship between free T3 and obesity, therefore, there are a number of factors that contribute to free T3 levels in obese subjects. These factors could vary among different subjects with same weight, like body composition, underlying thyroid diseases, iodine intake, etc.

Another hypothesis is a neuroendocrine dysfunction resulting in an abnormal secretion rate of TSH could be the cause of elevated TSH concentrations in obese subjects. It has been observed that D2, which is the main pituitary deiodinase isoenzyme, and its activity, is the key point to release TSH under T3 control, but does not work appropriately in these individuals. This mechanism may be damaged according to the observation that pituitary D2 expression does not reach the normal range in obese subjects. In addition, an Ala92 D2 variant in humans induces obesity and insulin resistant state in comparison with wild type 92Thr D2⁽²⁰⁾. Consequently, a resetting of the HPT axis, and not merely insufficient TH levels, seems to be a key factor that shifts the energy expenditure equation in obese subjects.

The adipocyte-derived hormone, leptin, may be at the origin of this dysfunction⁽²¹⁾, leptin itself directly stimulates TRH secretion, and subsequently TSH and TH⁽²²⁾. In addition, leptin has shown to have a direct inhibitory effect on several components involved in TH production from thyrocytes⁽²³⁾; and, leptin may directly affect the sensitivity of the thyrotroph or the thyrocyte⁽²⁴⁾.

A rise in serum TSH levels is usually interpreted as a hypothyroid status, but may also be the result of an effort to stimulate the thyroid and, therefore, the induction of gland over activity,

some investigators have suggested the existence of partially bioinactive TSH in obese subjects, although this hypothesis is very speculative⁽²⁵⁾.

Other authors suggest that there may be certain TH resistance, as well as decreased T3 receptors in obese subjects⁽²⁶⁾.

The study showed positive significant correlation between waist circumference and age that may be explained by the effect of sex hormone estrogen, since the adipocytes shows receptors attenuated to the estrogen, estrogen has control on the lipoprotein lipase and reduce adipocytes growth in females, this effect of estrogen suggests that a decrease in its secretion may promote accumulation of intra abdominal adipose tissue once menopause occurs in women, visceral adipose tissue contains greater number of large adipocytes while subcutaneous adipose tissue contain small adipocytes which are more insulin sensitive and have high avidity for free fatty acids and TGs uptake preventing their deposition in non-adipose tissue^(27,28). Also the study showed negative significant correlation between T3 and age and this finding is in agreement with previous study⁽²⁹⁾.

The American Thyroid Association advocates for more frequent and earlier screening, recommending measurement of thyroid stimulating hormone (TSH) beginning at age 35 and every 5 years thereafter⁽³⁰⁾. One of the most compelling reasons to screen for hypothyroidism is to reduce the risk of the potential consequences of SCH, since approximately 33-55% of patients went on to develop overt hypothyroidism within 10-20 years, and while the development of overt hypothyroidism or cardiovascular disease are two of the more severe potential consequences of SCH, the disease also has an impact on quality of life and has been associated with neuropsychiatric disease, defects in verbal memory and executive function⁽³¹⁾. The United States Preventive Services Task Force advocates screening of persons with familial thyroid disorders, obese individuals, pregnant women and patients with depression⁽³²⁾. The cost-effectiveness of screening for SCH compares favorably with other generally accepted preventive medical practices⁽³³⁾.

CONCLUSION:

The frequency of SCH is more in centrally obese women. Assessment of thyroid function must be regarded as part of the screening program in obese.

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SUBCLINICAL HYPOTHYROIDISM

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