

## Original Research Article

# Relationship of thyroid function with body fat, waist circumference, sub-cutaneous and visceral adipose tissue in eu-thyroid female subjects

Sanhita Mukherjee<sup>1\*</sup>, Debasis Deoghuria<sup>2</sup>, Diptakanti Mukhopadhyay<sup>3</sup>

<sup>1</sup>Department of Physiology, Calcutta National Medical College, Kolkata, West Bengal, India

<sup>2</sup>Department of Radiodiagnosis, B.S. Medical College, Bankura, West Bengal, India

<sup>3</sup>Department of Community Medicine, College of Medicine and Sagar Dutta Hospital, Kamarhati, Kolkata, West Bengal, India

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### \*Correspondence:

Dr. Sanhita Mukherjee,

E-mail: [drsanhita@gmail.com](mailto:drsanhita@gmail.com)

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## ABSTRACT

**Background:** The relationship between thyroid function, body weight and central obesity in euthyroid individuals has been given a great medical concern. Central abdominal adiposity can be divided into adipose tissue present in subcutaneous areas (SCAT) and visceral areas (VAT). The type of adiposity may be implicated in the associations of thyroid function parameters with obesity. The aim of the present study was to evaluate thyroid function and its possible relationship with BMI, body fat percent, waist circumference, SCAT and VAT in eu-thyroid female subjects.

**Methods:** Randomly selected eu-thyroid female subjects were included in this study. Their BMI was estimated by metric method, body fat percent was measured by Harpenden skin fold caliper. Ultrasound (US) was used to assess regional adiposity. Serum TSH was measured from fasting serum sample by Enzyme-linked-immuno-sorbant (ELISA) Assay. Data was analysed by SPSS (version 18).

**Results:** A positive linear association was found between serum TSH level and BMI, body fat percent, waist circumference and VAT. ( $r=0.342$ ,  $p < 0.002$ ,  $r=0.628$ ,  $p < 0.00$ ,  $r=0.289$ ,  $p < 0.009$ ,  $r=0.375$ ,  $p < 0.000$ ). No significant association was found with SCAT and TSH. There is gradual increase in serum TSH values among three BMI groups i.e. normal weight (BMI  $< 23$  kg/m<sup>2</sup>), over-weight (BMI 23.00-24.99 kg/m<sup>2</sup>), and obese (BMI  $> 25$  kg/m<sup>2</sup>) females. Body fat percentage, BMI and VAT were found to be significant independent predictors of TSH.

**Conclusions:** Selective reduction of visceral fat may induce greater beneficial effects on the parameters of thyroid hormones than subcutaneous fat reduction.

**Keywords:** Body fat, TSH, SCAT, VAT

## INTRODUCTION

The relationship between thyroid function and body weight in euthyroid individuals has been given a great medical concern. Evidence suggests that slight variations in thyroid function, even as indicated by tests that are within laboratory reference ranges, contribute to the development of regional obesity and the tendency to gain weight.<sup>1,2</sup> Higher serum TSH concentrations are

consistently found in obese children and adults compared with normal-weight individuals.<sup>3-6</sup> Several previous studies have reported associations between thyroid function parameters such as TSH and thyroid hormone levels, within the normal range, and changes in BMI and fat distribution.<sup>7-10</sup> Few studies reported that central fat accumulation, as assessed by waist circumference measurement, was positively and independently associated with TSH and free triiodothyronine (fT3)

levels in overweight and obese euthyroid women.<sup>10</sup> However, these results have not been confirmed by all investigators; Manji et al. reported no associations of TSH or fT4 levels with BMI in euthyroid individuals.<sup>11</sup>

Obese individuals vary in their body fat distribution. There are differences between adipose tissues present in subcutaneous areas (SCAT) and visceral adipose tissue (VAT) present in the abdominal cavity.<sup>12</sup> These include anatomical, cellular, molecular, physiological, clinical and prognostic differences. Anatomically, VAT is present mainly in the mesentery and omentum, and drains directly through the portal circulation to the liver. VAT compared with SCAT is more cellular, vascular, innervated and contains a larger number of inflammatory and immune cells, lesser preadipocyte differentiating capacity and a greater percentage of large adipocytes.<sup>12</sup>

It is well known that adipose tissue and especially visceral fat is implicated in the pathogenesis of the metabolic syndrome (MS). Subjects with increased central fat distribution are at higher risk for the development of cardiometabolic disease.<sup>13</sup> Visceral and subcutaneous fat (SF) expresses thyroid hormone receptors as well as TSH receptors that may also directly influence various functions of adipose cells.<sup>14-18</sup> However, it is not known whether the type of adiposity could be implicated in the associations of thyroid function parameters with obesity.

The aim of the present study was to evaluate thyroid function and its possible relationship with BMI, body fat percent, waist circumference, SCAT and VAT in euthyroid female subjects.

**METHODS**

This descriptive cross-sectional study was carried out at B. S. Medical College, Bankura, West Bengal, over a period of one year (January 2014-July 2015). Institutional ethical committee clearance and informed consent from all the subjects were obtained.

All the eu-thyroid female subjects attending Biochemistry Department for testing their thyroid profile during the study period were included in this study provided they have fulfilled the following inclusion criteria. Inclusion criteria for the subjects were: no significant clinical abnormalities on physical examination, no history of intake of lipid-lowering, hypoglycemic, antihypertensive drugs, no history of cardiovascular or respiratory disease, normal ECG (Electrocardiogram), normal fasting blood sugar level (<6-10m mol/l), normal systolic blood pressure (<130mmHg), normal diastolic blood pressure (<85mmHg) for at least three measurement.

A total of 103 eu-thyroid female subjects (i.e. TSH level within 0.4µIU/ml to 3µIU/ml) 19 who fulfilled the study criteria were included in the study. Body Mass Index and Body fat percent were measured in these subjects.

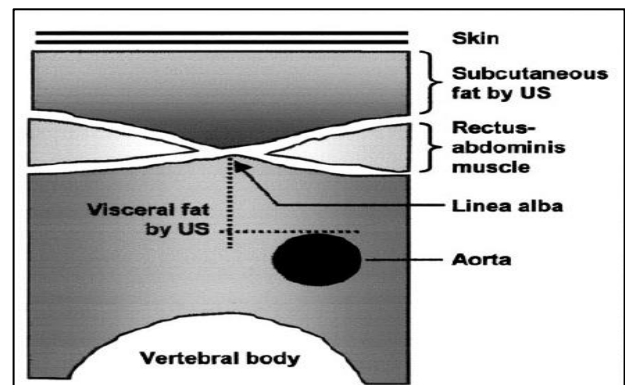
Body Mass Index was estimated by metric method.<sup>20</sup> The standing height of the subjects was measured with the same stadiometer, without footwear; to the nearest centimetre. Weight was measured, which was the nearest to 0.1kg, with the subjects in the standing position, before lunch, with light clothes and without footwear, by using a standardized weighing scale.<sup>21</sup>

**Table 1: Body density equations (Linear regression equations; Durnin and Wormersley).**

Body Density= C [M (log10 Sum of all four skin folds)]

Male	17-19 yrs	20-29 yrs	30-39 yrs	40-49 yrs	50+ yrs
C	1.1620	1.1631	1.1422	1.1620	1.1715
M	0.0630	0.0632	0.0544	0.0700	0.0779
Female	16-19 yrs	20-29 yrs	30-39 yrs	40-49 yrs	50+ yrs
C	1.1549	1.1599	1.1423	1.1333	1.1339
M	0.0678	0.0717	0.0632	0.0612	0.0645

Fat % = [(4.95/Body Density)-4.5]\*100



**Figure 1: Abdominal adipose tissue landmark. (A): anatomical landmark of abdominal adipose tissue, (B): illustration of abdominal adipose tissue and anatomical landmarks used for ultrasound measurement.<sup>24</sup>**

Depending on their BMI values, the subjects were classified into three groups. The subjects with a BMI value of less than 23 (kg/m<sup>2</sup>) was be classified as normal

weight, subjects with a BMI value between 23 to 24.99 (kg/m<sup>2</sup>) was classified as the overweight group and those who have a BMI value more than 25 (kg/m<sup>2</sup>) was classified as obese.<sup>21,22</sup> Waist circumference was measured at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest, using a stretch resistant tape.<sup>22</sup>

Harpenden skin fold caliper was used to measure percent of body fat. The four-site system was used in female subjects. Site 1-biceps, site 2- triceps, site 3- sub-scapular, site 4- supra-iliac. To calculate % Body fat linear regression equations of Durnin and Wormersley was used.<sup>23</sup>

Authors used ultrasound (US), a reliable low-cost method, to assess regional adiposity. All ultrasonographic procedures were performed by the same examiner using a 3.5-MHz probe located 1 cm from the umbilicus. Two US measurements of intraabdominal (“visceral”) and subcutaneous fat were taken. US-determined subcutaneous fat was defined as the distance between the skin and external face of the rectus abdominis muscle, and visceral fat was defined as the distance between the internal face of the same muscle and the anterior wall of the aorta (Figure 1).<sup>24</sup> The intra examination coefficient of variation for US was 0.8%.

Serum TSH was estimated by Enzyme-linked-immunosorbant assay (ELISA). Five ml of cord blood samples were collected from the peripheral veins in sterile test tubes. The serum separated by centrifugation was used for quantitative estimation of TSH, total T3, total T4 by a micro plate immuno-enzymatic assay (Ranbaxy). The intra and inter-assay coefficient of variation (CV) for TSH estimation were 4.33% and 7.5% respectively and the sensitivity limit was 0.078 μ IU/ml. That for total T3 was 5.73% and 6.7% respectively with the sensitivity limit 0.04 ng/ml and total T4 were 4.7% and 5.4% respectively with the sensitivity limit 0.4 μg/dl.

The collected data was analyzed with SPSS (version 18) statistical package. Pearson’s correlation test was used to see the association between TSH, BMI, Body fat Percent, WC, Subcutaneous and visceral fat.

The study population were further subdivided into three groups normal weight (BMI<23 kg/m<sup>2</sup>), over-weight (BMI 23.00-24.99 kg/m<sup>2</sup>) and obese (BMI>25 kg/m<sup>2</sup>) in

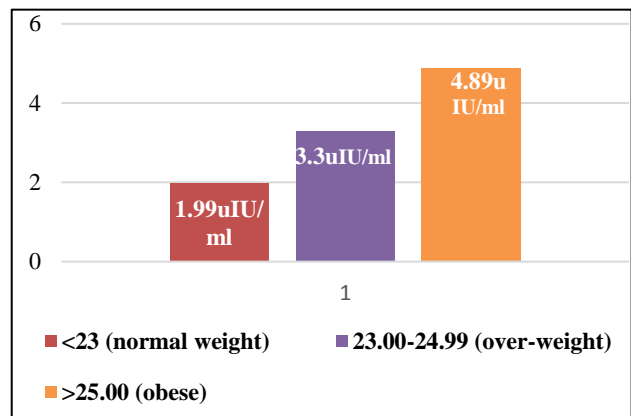
accordance with their BMI. Analysis of Variance (ANOVA) Test among the above three groups was done to see the changes of TSH level with increasing body mass index.

As TSH, BMI, body fat could be affected by a third factor, which according to the observation could be age, author included age as independent variable in multiple regression analysis.

Multiple linear regression analysis was done to show the relation between TSH level, body fat percentage, BMI, SCAT, VAT and age of the study participants.

**RESULTS**

A total of 103 eu-thyroid female subjects were included in the study. Their mean age was 56 years (Range 30-82). A significant positive association was observed between serum TSH and BMI (r=0.342, p<0.002), Body fat percent (r=0.628, p <0.000), WC (r=0.289, p <0.009),VAT (r=0.375, p <0.000) in eu-thyroid female subjects (Table 2) but no significant association was found with SCAT (r=0.105, p=0.316).



**Figure 2: Serum TSH values in normal weight, over-weight and obese eu-thyroid females.**

There are significant (p <0.003) inter-group variations among BMI and serum TSH concentration (Table 3). Serum TSH values gradually increases among three BMI groups i.e. normal weight (BMI <23 kg/m<sup>2</sup>; TSH Mean ±SD: 1.99±1.49), over-weight (BMI 23.00-24.99 kg/m<sup>2</sup>; TSH Mean ±SD: 3.30±2.78), and obese (BMI >25 kg/m<sup>2</sup>; TSH Mean ±SD: 3.28 ±2.29) females (Figure 2).

**Table 2: The association between BMI, body fat percent, waist circumference, sub-cutaneous Adipose tissue, visceral adipose tissue and serum TSH in eu-thyroid female subjects.**

	BMI (kg/m <sup>2</sup> )	% Body fat	WC (cm)	SCAT (cm)	VAT (cm)	
TSH (μ IU/ml)	Pearson correlation (r)	0.342***	0.628***	0.289**	0.105	0.375**
	Sig. (2 tailed)	<0.002	0.000	.009	0.316	0.000
	n	103	103	93	93	93

\*\*. Correlation is significant at the 0.01 level (2-tailed).

In order to control the effect of a third factor, e.g. age, between the association of serum TSH and BMI, age was

included as an independent variable in multiple regression analysis.

**Table 3: Serum TSH concentration in normal weight, over-weight and obese eu-thyroid females.**

BMI (kg/M <sup>2</sup> )	N	TSH(μ IU/ml) Mean± S.D	Calculated F ratio	Significance
<23 (normal weight)	79	1.99±1.49	6.176	0.003**
23.00-24.99 (over-weight)	8	3.30±2.78		
>25.00 (obese)	16	3.28±2.29		

**Table 4: Multiple linear regression showing relation between TSH level, body fat percentage and age of the study participants.**

Variable	Unstandardized coefficient		
	B	Std. Error	Sig.
Constant	-0.512	0.798	0.523
B. Fat%	0.113	0.039	0.005
Age in yrs	-0.003	0.019	0.879

Dependent variable: TSH (Uiu/ml); TSH = - 0.512 + 0.113 b.fat% - 0.003 Age in yrs, body fat percentage is a significant predictor of TSH but age is not.

It shows Body fat percentage and BMI were significant independent predictors of TSH, but age was not. (TSH = - 0.512 + 0.113 b. fat % - 0.003 age in yrs) (Table 4). Abdominal fat was further subdivided into SCAT and VAT. Multiple linear regression analysis was done to show the relation between TSH level, body fat percentage, BMI, SCAT, VAT and age of the study

participants. Linear regression model shows VAT is positive and independent predictor of TSH (TSH = 0.481 - 0.039 (subcutaneous fat) + 0.742 (Visceral fat). Inclusion of age did not show significant R2 change, and so, was not included in the final model (Table 6).

**Table 5: Multiple linear regression showing relation between TSH level, body mass index and age of the study participants.**

Variable	Unstandardized coefficient		
	B	Std. Error	Sig.
Constant	-1.045	0.989	0.293
BMI	0.128	0.047	0.008
Age in yrs	0.025	0.015	0.103

Dependent variable: TSH (Uiu/ml); TSH = -1.045 + 0.128 BMI + 0.025 Age in yrs BMI is a significant predictor of TSH but age is not. Upper two tables demonstrated model fit R-square change and Sum of squares in regression showed that body fat % is a better predictor.

**Table 6: Linear Regression model showing relation between TSH level, SCAT and VAT of the study participants.**

Variable	Unstandardized coefficients		t	Sig.	95.0% Confidence Interval for B	
	B	Std. Error			Lower bound	Upper bound
Constant	0.481	0.573	0.838	0.404	-0.659	1.620
Subcut. Fat (cm)	-0.039	0.342	-0.115	0.908	-0.718	0.639
Visceral fat (cm)	0.742	0.201	3.685	0.000	0.342	1.143

TSH = 0.481 - 0.039 (subcutaneous fat) + 0.742 (visceral fat)\* Inclusion of age did not show significant R2 change, and so, was not included in the final model.

## DISCUSSION

In the present study, author have found that although in the normal range, serum TSH is positively associated with BMI and body fat percent in eu-thyroid female subjects. This finding is in agreement with the study of Nyrnes A et al, who showed serum TSH within the normal range to be significantly and positively associated with BMI in non-smoking men and women.<sup>25,26</sup> Knudsen N et al, also showed small differences in thyroid function

may be important for Body Mass Index and the occurrence of obesity in the population.<sup>8</sup> Although Manji et al. reported no associations of TSH or fT4 levels with BMI in euthyroid individuals.<sup>11</sup>

Furthermore, there are significant inter-group variations among BMI and TSH concentration in the study. Serum TSH values gradually increases among three BMI groups i.e. normal weight, over-weight and obese. This result is in contrast with the study performed by Bakiner O et al,

that showed no association regarding BMI categories and plasma TSH levels in their euthyroid cohort, overweight, obese, morbid obese, and normal weight subjects.<sup>27</sup> But they mentioned that absence of correlation between plasma TSH levels and obesity in their study does not mean that TSH and thyroid hormones have no effect on adiposity.

In order to control the effect of a third factor, e.g. age, between the association of serum TSH and BMI, author included age as an independent variable in multiple regression analysis. Authors found body fat percentage and BMI were significant independent predictors of TSH but age is not. This is in accordance with Nyrenes A et al, who reported age is an unlikely explanation for the association between TSH and BMI.<sup>26</sup>

To have a better idea of association between serum TSH and regional adiposity markers author further subdivided abdominal fat into SCAT and VAT and measured it by US which has proved to be a suitable non-invasive and reliable tool for quantifying abdominal fat as useful as CT.<sup>28</sup> Present study revealed one interesting finding that TSH is significantly and positively associated with VAT but no significant association was found with SCAT and TSH. Furthermore, VAT is positive and independent predictor of TSH. Very few previous studies focused on this topic and one of such study even contradict this report as they did not find any significant association between Visceral Fat and fT4 or TSH levels.<sup>29</sup> But in the subgroup of overweight and obese subjects they found the inverse association of Subcutaneous Fat layer with fT4 levels.

It is now well known that VAT is associated with increase cardiovascular risk.<sup>30</sup> SCAT does not pose the same health danger as the VAT and visceral fat expresses thyroid hormone receptors as well as TSH receptors that may also directly influence various functions of adipose cells.<sup>14-18</sup>

All forms of weight loss affect visceral fat more than subcutaneous fat.<sup>30</sup> Hence Selective reduction of visceral fat may induce greater beneficial effects on the parameters of thyroid hormones than subcutaneous fat reduction.

The present study has few limitations. Present study is a cross-sectional study. A longitudinal study with more sample size will give better idea of the relationship between thyroid profile and regional adiposity markers.

## CONCLUSION

There is significant positive association of TSH with BMI, Body fat percent, WC and VAT in eu-thyroid female subjects. No significant association was found between TSH and SCAT. Hence selective reduction of visceral fat may induce greater beneficial effects on the

parameters of thyroid hormones than subcutaneous fat reduction.

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