

CORRELATION BETWEEN OBESITY AND THYROTROPIN (TSH) IN CLINICALLY EUTHYROID SUBJECTSMadhumita De¹, Abhijit Rakshit²¹Assistant Professor, Department of Physiology, R. G. Kar Medical College, Kolkata, West Bengal, India.²Associate Professor, Department of Obstetrics and Gynaecology, R. G. Kar Medical College, Kolkata, West Bengal, India.**ABSTRACT****BACKGROUND**

Thyroid stimulating hormone (TSH, Thyrotropin) induces adipogenesis and adipokine production directly and may contribute to the evolution of obesity, independent of any involvement of the thyroid gland. This study has been conducted to evaluate the association of minor disturbances of thyroid function with changes in obesity indicators like Body Mass Index (BMI) & Waist-Hip Ratio (WHR). We wanted to assess the correlation between the serum TSH level and the various obesity indicators.

METHODS

This study was conducted in the Department of Physiology, MGM Medical college, Kishanganj, Bihar, in collaboration with the Department of Biochemistry and Department of Gynaecology & Obstetrics, between 2014 and 2016, among 200 medical and paramedical students (100 males and 100 females) attending classes in the Department of Physiology, found to be clinically euthyroid with no family history of thyroid disorder and no history of taking any medication which may affect the thyroid profile.

RESULTS

In this study the average height of males (1.76 ± 0.055 metres) is greater than the average height of females (1.58 ± 0.077 metres). Average weight is also higher in males (85.14 ± 11.181 kgs) than females (61.20 ± 11.963 kgs). Therefore, in this study BMI is more in males (27.61 ± 4.790 kg/m²) in comparison to females (25.59 ± 5.109 kg/m²). This observation regarding BMI contradicts the findings of Kota SK et al,¹⁶ Jung CH et al¹⁵ studies where the BMI is more in females than in males, whereas observation of Mahanta M et al¹⁷ is that BMI of males (21.41 ± 2.197 kg/m²) was slightly more than that of females (21.36 ± 2.995 kg/m²) which to some extent corresponds with the findings of this study. Average Waist Circumference (WC) of males (0.89 ± 0.093 metres) is greater than the average WC of females (0.77 ± 0.107 metres) and average Hip Circumference (HC) is greater in males (1.04 ± 0.067 metres) than females (0.97 ± 0.102 metres) in this study. Therefore, it has been observed that Waist-Hip Ratio (WHR) is more in males (0.86 ± 0.057) than in females (0.78 ± 0.048) in this study. Result of WHR in our study corroborates with observation of Mahanta M et al¹⁷ where WHR in male group (0.84 ± 0.059) was more than female group (0.77 ± 0.048).

CONCLUSIONS

There is no correlation between BMI and serum TSH levels in female subjects, whereas there is moderate direct correlation between TSH level and BMI, TSH level and Weight in male group and there is good inverse correlation between TSH level and WHR in female group and moderate inverse correlation between TSH level and Weight, TSH level and Waist Circumference in female subjects.

KEY WORDS

TSH, Body Mass Index (BMI), Waist Hip Ratio (WHR).

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BACKGROUND

Thyroid stimulating hormone (TSH, Thyrotropin), secreted by the thyrotrope cells of the anterior pituitary, plays a pivotal role in the control of the thyroid axis and serves as the most useful physiologic marker of thyroid action.¹

Emerging evidence suggests that thyrotropin induces adipogenesis and adipokine production directly and may contribute to the evolution of obesity, independent of any involvement of the thyroid gland.²

Recent studies in man and other mammalian species have shown that adipocytes and preadipocytes possess

thyrotropin receptors.^{3,4} The signals generated by thyrotropin in adipocytes is mediated by the activation of c-AMP dependant protein kinase.⁵ Studies in vitro and in vivo demonstrate that the action of thyrotropin via its receptors in fat tissues induces differentiation of preadipocytes into adipocytes and expansion of adipose tissue i.e. adipogenesis.^{3,6}

Adipose tissue is a major endocrine gland, producing numerous adipokines, which have metabolic and inflammatory effects on other tissues.^{7,8}

Schaffer A et al⁴ proposed that a hypothalamic- pituitary- adipose tissue axis exists. The positive relationship between serum TSH and adiposity would be consistent with this concept in a downstream sense. Yet, such an axis would require a feedback system. Hence the positive relationship between serum TSH and adiposity could also be interpreted in the reverse. Among the adipokines, extensive information is available on the inhibition of appetite by Leptin, dominantly by acting on the hypothalamus. A positive correlation has been reported between serum levels of Leptin and TSH.^{10,11}

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Corresponding Author:

Dr. Abhijit Rakshit,

Block-2, Flat-3c,

Shakuntala Garden, 609 Laskarhat,

Kolkata-700039, West Bengal, India.

E-mail: drabhijitr81@gmail.com

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In recent years, there has been an increasing focus on subclinical thyroid dysfunction. Subclinical hypothyroidism, defined as an elevated serum TSH but with serum free thyroxine levels within the normal range, is associated with dyslipidaemia.¹²

As overweight is associated with increased morbidity and disability, a study of relationship between thyroid function and body weight might be of importance.¹³ Until now, only a few epidemiological studies evaluating the association between the levels of thyroid hormones and TSH with body weight and BMI were carried out.

The Dan Thry study¹⁴ showed a positive correlation between BMI and category of TSH. Obesity (BMI>30 kg/m²) and serum TSH levels were significantly associated in this cohort study. A study showed that TSH was positively associated with waist circumference.¹⁵ Another study found that patients with hypothyroidism exhibited higher waist-to-hip ratios, an index of obesity.¹⁶

It is obvious that thyroid dysfunction affects body weight, however, possible association of minor disturbances of thyroid function with changes in various anthropometric measurements related to obesity – Body Mass Index (BMI) & Waist-Hip Ratio (WHR) need to be elucidated.

Thus, the present study “Correlation between obesity & thyrotropin (TSH) in clinically euthyroid subjects” was undertaken.

Aims & Objectives

1. To assess various anthropometric measurements related to obesity Height, Weight, Body Mass Index (BMI), Waist circumference, Hip circumference, Waist Hip Ratio (WHR) in the study population (Medical and Paramedical Students).
2. To measure the serum TSH level of the same subjects.
3. To assess the correlation between the serum TSH level and the various anthropometric measurements.

METHODS

The present study was conducted in the Department of Physiology, MGM Medical College, Kishanganj, Bihar in collaboration with the Department of Biochemistry and G & O after getting ethical clearance. The period of study was between May 2014 to April 2016. The study was conducted among 200 medical and paramedical students (100 males and 100 females) attending classes in the Department of Physiology. The purpose and procedure of the study was explained to all participants. Detailed history was taken, general and systemic examinations were done.

Exclusion Criteria

1. Present or past history of any thyroid disorder.
2. Family history of any thyroid disorder.
3. History of intake of any medication which may affect the thyroid hormone profile such as, glucocorticoids, anti-thyroid drugs, thyroid hormone replacement, Oestrogen and Progesterone preparations.
4. History or clinical examination suggestive of any signs or symptoms related to thyroid disorder.

Statistical Methods

The data collected was tabulated and subjected to statistical analysis. All data were expressed as Mean ± SD, an unpaired t

test, Correlations coefficients were calculated using MS Excel. Software used Statistica version 6 [Tulsa, Oklahoma: StatSoft Inc., 2001] & MedCalc version 11.6 [Mariakerke, Belgium: Med Calc Software 2011].

The formula of Body Mass Index (BMI) calculation:

$$\frac{\text{Weight (in kilograms)}}{(\text{Height in meters})^2}$$

Waist – Hip Ratio (WHR) will be calculated by the formula:

$$\frac{\text{Waist circumference (in metres)}}{\text{Hip circumference (in metres)}}$$

After taking history and conducting general and systemic examinations, subjects found to be clinically euthyroid were included in the study. Written informed consent was taken from all the subjects. For each subject, after measuring height, weight, waist circumference and hip circumference, blood samples were collected for estimation of TSH. Waist circumference was measured at the midpoint between the lower border of the rib cage and the iliac crest. The hip circumference measurement is taken at the level of the greatest protrusion of the gluteal (buttock) muscles. Height was measured by making the subject stand against a metric measuring scale. The subjects were asked to stand bare feet on a flat floor against the scale with heels, buttocks, shoulders and occiput touching the scale. The subjects were asked to keep their heads erect with eyes aligned horizontally and ears vertically without any tilt. With the help of a ruler, the topmost point of the vertex was identified on the scale.

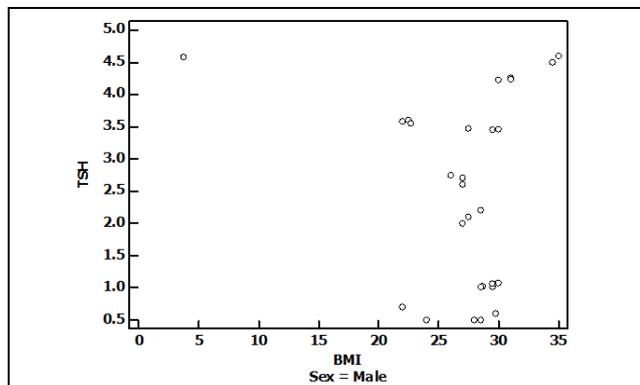
RESULTS

Group	Males + Females (200)	Males (100)	Females (100)	Comparison of “p” Value between Male & Female
Height (Metres)	1.67± 0.11	1.76 ± 0.055	1.58± 0.077	<0.001
Weight (Kg)	73.17 ± 16.66	85.14 ± 11.181	61.20 ± 11.963	<0.001
BMI (Kg/m ²)	26.60 ± 5.03	27.61 ± 4.790	25.59 ± 5.109	0.044
WC (Metres)	0.83 ± 0.12	0.89 ± 0.093	0.77 ± 0.107	<0.001
HC (Metres)	1.01 ± 0.09	1.04± 0.067	0.97 ± 0.102	<0.001
WHR	0.82 ± 0.06	0.86 ± 0.057	0.78 ± 0.048	<0.001
TSH (mIU/ml)	2.66 ± 1.28	2.38 ± 1.481	2.95 ± 0.982	0.058

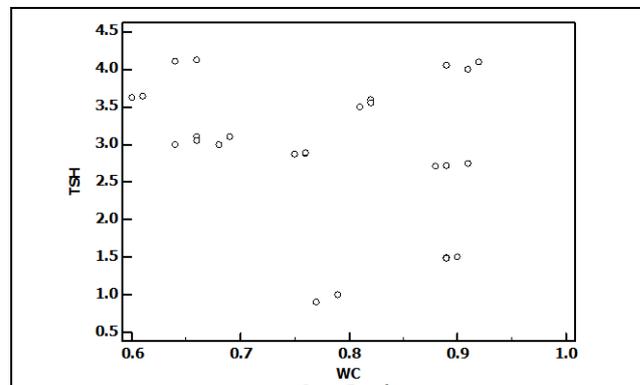
Table 1. Mean & Standard Deviation of Anthropometric Parameters Related to Obesity and TSH Values Among the Subjects

Values indicate mean ± standard deviation

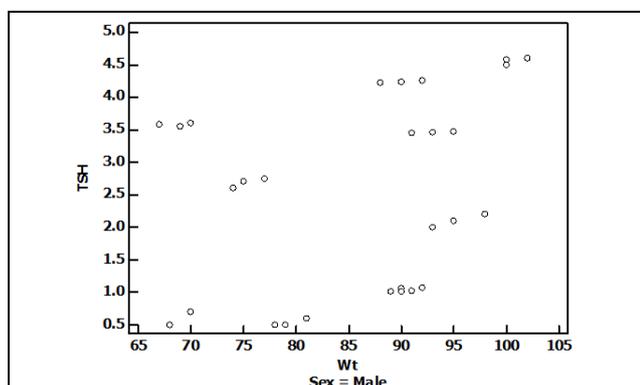
Table 1 depicts mean values of anthropometric parameters like Height, Weight, BMI, Waist Circumference (WC), Hip Circumference (HC), Waist Hip Ratio (WHR) are all on the higher side in males in comparison to females. Whereas TSH level is too some extent lower in males in compare to females. Regarding comparison of “p” value between males and females, it has been seen that “p” value is significant in Height, Weight, Waist Circumference, Hip circumference and Waist Hip Ratio (p <0.001).



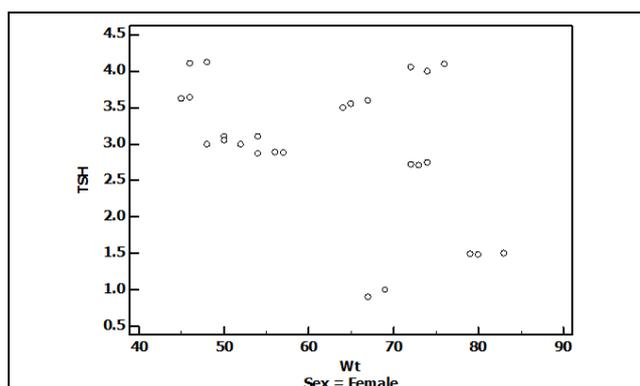
Picture 2. Shows Moderate Direct Correlation [Spearman's Coefficient of Rank Correlation (ρ)=0.304] between TSH Level & BMI in Male Group



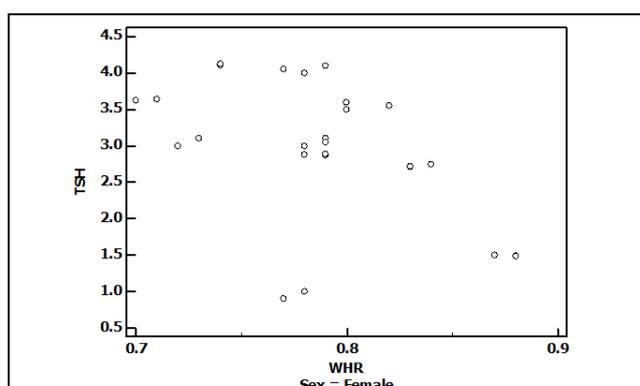
Picture 6. There is Moderate Inverse Correlation (ρ =-0.314) between TSH Level & Waist Circumference (WC) in Female Group



Picture 3. There is Moderate Direct Correlation (ρ =0.385) between TSH Level & Weight in Male Group



Picture 4. It Shows Moderate Inverse Correlation (ρ = -0.495) between TSH Level & Weight (Wt.) in Female Group



Picture 5. There is Good Inverse Correlation (ρ =-0.521) between TSH Level & Waist Hip Ratio (WHR) in Female Group

The reading was recorded to the nearest centimetre. Weight was recorded using weighing machine (Adult type) to the nearest kilogram. Subjects were asked to remove shoes and any bulky clothing before recording of weight. Estimation of serum TSH was done in Human serum by Chemiluminescence Immunoassay (CLIA). It is an Immunoenzymometric assay.

DISCUSSION

In this study, (Table 1) average height of males (1.76 ± 0.055 metres) is greater than the average height of females (1.58 ± 0.077 metres). Average weight is also higher in males (85.14 ± 11.181 kgs) than females (61.20 ± 11.963 kgs). Therefore in this study BMI is more in males (27.61 ± 4.790 kg/m²) in comparison to females (25.59 ± 5.109 kg/m²). This observation regarding BMI contradicts the findings of Kota SK et al,¹⁶ Jung CH et al¹⁵ studies where the BMI is more in the females than males, whereas observation of Mahanta M et al¹⁷:- BMI of males (21.41 ± 2.197 kg/m²) was slightly more than the females (21.36 ± 2.995 kg/m²), to some extent corresponds with the findings of this study.

Average Waist Circumference (WC) of males (0.89 ± 0.093 metres) is greater than the average WC of females (0.77 ± 0.107 metres) and average Hip Circumference (HC) is greater in males (1.04 ± 0.067 metres) than females (0.97 ± 0.102 metres) in this study (Table 1). Therefore, it has been observed Waist-Hip Ratio (WHR) is more in males (0.86 ± 0.057) than in females (0.78 ± 0.048) in this study. Result of WHR in our study corroborates with observation of Mahanta M et al¹⁷ where WHR in male group (0.84 ± 0.059) was more than female group (0.77 ± 0.048).

The present study found that there is no correlation between serum TSH level and height, hip circumference in total subjects, male and female group. On contrary to common observations in various studies, it has been seen that there is no correlation between BMI and serum TSH level in female subjects, whereas there is moderate direct correlation between TSH level and BMI (Pic. 2) and TSH level and Weight (Pic. 3) in male group and there is good inverse correlation between TSH level and WHR in female group (Pic. 5) and, moderate inverse correlation between TSH level and Weight (Pic. 4) and TSH level and Waist Circumference (Pic. 6) in female subjects.

Bastemir M et al² found positive and significant correlation between serum TSH level with body weight ($r=0.231$, $p<0.001$), BMI ($r=0.270$, $p<0.001$), waist

circumference ($r = 0.219$, $p=0.001$) in total study group, whereas in the present study TSH level has moderate direct correlation with BMI ($\rho=0.304$, $P=0.0321$) and Weight ($\rho = 0.385$, $P=0.0058$) only in male group and good inverse correlation with WHR ($\rho=-0.521$, $P=0.0001$) and moderate inverse correlation with Weight ($\rho = -0.495$, $P=0.0003$) and Waist Circumference ($\rho=-0.314$, $P=0.0266$) in female group.

Kundsen N et al¹³ found a positive association between BMI and serum TSH level ($p<0.001$), a negative association between BMI and serum free T_4 level and no association between BMI and free T_3 level. Therefore, their study suggested that even slightly elevated serum TSH levels are associated with an increase in the occurrence of obesity despite of normal thyroid function. It corroborates with the findings in male population: moderate direct correlation between TSH level and BMI.

Jung CH et al¹⁵ performed a study with 66,260 Korean population. They found that overt and subclinical, both groups of hypothyroidism exhibited higher waist to hip ratios, an index of obesity. Whereas in the present study (In 100 clinically euthyroid subjects), there is good inverse correlation between serum TSH level and WHR in female group and no correlation in male group.

Galofre JC et al¹⁸ performed a study over 144 euthyroid obese male patients (Mean BMI 41.8 kg/m²). They have found a positive correlation between BMI and TSH ($r=0.22$; $p<0.05$), as well as between serum baseline Insulin (>10 mu/l) and TSH concentration ($r=0.27$; $p<0.05$). It corroborates with the present study where there is moderate direct correlation between TSH level and BMI specially in male group.

Shon HS et al¹⁹ studied a total of 1572 euthyroid women in a cross-sectional study. They sought to evaluate thyroid function (Free T_4 , TSH) and its possible relationship with BMI and lipid profiles in euthyroid subjects. After adjustment for age and smoking, TSH was not correlated with BMI which echoes our findings where TSH level has no relation with BMI in female group.

Hari Kumar KVS et al²⁰ showed that elevated TSH level (between 4.5 – 10 m IU/l) with normal T_3 , T_4 was seen in 4/20 overweight and 9/30 of obese children ($p=0.5219$). The mean TSH was comparable in both the groups (3.22 ± 3.1 m IU/L vs. 3.63 ± 2.2 m IU/L, $p = 0.3491$). Overall TSH showed no correlation with BMI ($r=0.0014$, $p=0.9924$). They concluded that the preliminary data did not show any relation between severity of obesity and TSH level. In the present study there is no correlation between TSH level and BMI in female subjects but there is moderate direct correlation between TSH level and BMI in male group.

Ambrosi B et al²¹ evaluated serum TSH and free T_4 levels, anthropometric and metabolic parameters in 581 obese patients and they concluded that a relationship between thyroid function and overweight/ obesity condition seems to exist, mainly influenced by insulin resistance. Whether variations in TSH and/or thyroid hormones, within a normal range, can influence body weight or whether obesity per se can alter thyroid function cannot be stated so far. In present study there is a moderate direct correlation between serum TSH level and BMI, a marker for obesity, in male population but no relation in female group. Whereas another marker of obesity, WHR has moderate inverse correlation with BMI in female group.

Limitations

Our study was not designed to prove or disprove a direct role of thyrotropin in adiposity. It was at best a time bound cross-sectional observational study, taking advantage of the availability of structured clinical information on 100 medical and paramedical students selected at random. Only serum TSH has been estimated in study subjects. It is not evident clearly whether increased TSH levels favour the deposition of fat, or, on the contrary, whether excessive accumulation of fatty tissue increases TSH secretion. Other parameters like Serum levels of T_3 , T_4 , Serum Insulin level or plasma Leptin concentration also need to be measured to find out their effect on various anthropometric parameters. Also, study population is small in number. As this is a time-bound study, it was not possible to conduct this over a large population. Therefore, we cannot construct a cause-effect relationship with our observation. However, there is an urgent need to conduct a longitudinal, long term follow-up study over a large population to establish the reference values and cause-effect relationship between obesity and serum TSH level.

CONCLUSIONS

There is no correlation between BMI and serum TSH levels in female subjects, whereas there is moderate direct correlation between TSH level and BMI, TSH level and Weight in male group and there is good inverse correlation between TSH level and WHR in female group and moderate inverse correlation between TSH level and Weight, TSH level and Waist Circumference in female subjects.

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REFERENCES

- [1] Jameson JL, Weetman AP. Disorders of the thyroid gland. In: Fauci AS, Braunwald E, Kasper DL, et al. eds. Harrison's Principles of Internal Medicine. Vol. 2. 17th edn. New York: The McGraw-Hill 2008: p. 2224-47.
- [2] Bastemir M, Akin F, Alkis E, et al. Obesity is associated with increased serum TSH level, independent of thyroid function. *Swiss Med Wkly* 2007;137(29-30):431-4.
- [3] Sorisky A, Bell A, Gagnon A. TSH receptor in adipose cells. *Horn Metab Res* 2000;32(11-12):468-74.
- [4] Schaffler A, Binart N, Scholmerich J, et al. Hypothesis paper Brain talks with fat -- evidence for a hypothalamic-pituitary-adipose axis? *Neuropeptides* 2005;39(4):363-7.
- [5] Rosenbaum M, Hirsch J, Murphy E, et al. Effects of changes in body weight on carbohydrate metabolism, catecholamine excretion and thyroid function. *Am J Clin Nutr* 2000;71(6):1421-32.
- [6] Valyasevi RW, Harteneck DA, Dutton CM, et al. Stimulation of adipogenesis, peroxisome proliferator-activated receptor gamma (PPARgamma) and thyrotropin receptor by PPARgamma agonist in human orbital preadipocyte fibroblasts. *J Clin Endocrinol Metab* 2002;87(5):2352-8.

- [7] Rajala MW, Scherer PE. Minireview: the adipocyte -- at the crossroads of energy homeostasis, inflammation and atherosclerosis. *Endocrinology* 2003;144(9):3765-73.
- [8] Rondinone CM. Adipocyte-derived hormones, cytokines and mediators. *Endocrine* 2006;29(1):81-90.
- [9] Menendez C, Baldelli R, Camina JP, et al. TSH stimulates leptin secretion by a direct effect on adipocytes. *J Endocrinol* 2003;176(1):7-12.
- [10] Zimmermann-Belsing T, Brabant G, Holst JJ, et al. Circulating leptin and thyroid dysfunction. *Eur J Endocrinol* 2003;149(4):257-71.
- [11] Danese MD, Ladenson PW, Meinert CL, et al. Effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of literature. *J Clin Endocrinol Metab* 2000;85(9):2993-3001.
- [12] Visscher TLS, Seidell JC. The public health impact of obesity. *Ann Rev Public Health* 2001;22:355-75.
- [13] Kundsen N, Laurberg P, Rasmussen LB, et al. Small differences in thyroid function may be important for body mass index and the occurrence of obesity in the population. *J Clin Endocrinol Metab* 2005;90(7):4019-24.
- [14] De Pergola G, Ciampolillo A, Paolotti S, et al. Free triiodothyronine and thyroid stimulating hormone are directly associated with waist circumference, independent of insulin resistance, metabolic parameters and blood pressure in overweight and obese women. *Clin Endocrinol (Oxf)* 2007;67(2):265-9.
- [15] Jung CH, Sung KC, Shin HS, et al. Thyroid dysfunction and their relation to cardiovascular risk factors such as lipid profile, hsCRP and waist hip ratio in Korea. *Korean J Intern Med* 2003;18(3):146-53.
- [16] Kota SK, Meher LK, Jammula S, et al. Obesity and thyrotropinemia: association in Indian adults. *Thyroid Research and Practice* 2013;10(1):4-7.
- [17] Mahanta A, Choudhury B, Choudhury DS. Serum thyrotropin level in relation to obesity indicators in a clinically euthyroid population. *International Journal of Physiology* 2013;1:7-12.
- [18] Galofre JC, Pujante P, Abreu C, et al. Relationship between thyroid-stimulating hormone and insulin in euthyroid obese men. *Ann Nutr Metab* 2008;53(3-4):188-94.
- [19] Shon HS, Jung ED, Kim SH, et al. Free T4 is negatively correlated with body mass index in euthyroid women. *Korean J Intern Med* 2008;23(2):53-7.
- [20] Harikumar KVS, Verma A, Muthukrishnan J, et al. Obesity and thyrotropinemia. *Indian J Pediatrics* 2009;76(9):933-5.
- [21] Ambrosi B, Masserini B, Iorio L, et al. Relationship of thyroid function with body mass index and insulin resistance in euthyroid obese subjects. *J Endocrinol Invest* 2010;33(9):640-3.