JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

How to cite this article:
NAGILA A*, BHATT M*, POUDEL B*, MAHATO P*, GURUNG D*, PRAJAPATI S*,ARUN KUMAR ***,TAMRAKAR BK**.THYROID STIMULATING HORMONE AND ITS CORRELATION WITH LIPID PROFILE IN OBESE NEPALESE POPULATION.
Journal of Clinical and Diagnostic Research [serial online] 2008 August [cited: 2008 August4]; 2: 932-937.
Available from
http://www.jcdr.net/back_issues.asp?issn=0973-709x&year=2008&month=August &volume=2&issue=4&page=932-937 &id=283

ORIGINAL ARTICLE

Thyroid Stimulating Hormone and its Correlation with Lipid Profile in the Obese Nepalese Population

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ABSTRACT

Background and Objectives: Obesity is an epidemic across the globe, with its presence even in the developing countries. Obesity is associated with derangements in the lipid profile, which further increases the risk of coronary heart disease, diabetes mellitus, stroke and certain cancers like endometrial, colon, oesophageal and uterine. However, the association of obesity and thyroid stimulating hormone (TSH) is equivocal. The current study was undertaken

[1] To establish the correlation between serum TSH level and varying degrees of obesity depending on the body mass index (BMI).

[2] To evaluate the relationship between BMI and lipid profile.

Materials and Methods: Two hundred and thirty seven (183 obese and 54 controls) subjects were recruited for this study, with their ages ranging from 30-65 years, attending the Western Regional Hospital, a government referral centre in the Western region of Nepal. Subjects with a history of familial hypercholesterolaemia, hyperthyroidism, diabetes, hypertension, renal disease, cardiovascular disease and cancer, were excluded from the study. Anthropometric variables, lipid profiles and TSH levels were determined in the controls and obese subjects. Blood glucose, serum urea, serum creatinine and SGPT levels were also determined in the participants.

Result: Significant differences in the systolic blood pressure (SBP) and diastolic blood pressure (DBP) were observed between obese and non-obese subjects (SBP; $p<0.05$; DBP; $p<0.05$). Weight and WC and W/H ratios, significantly, were positively correlated with increasing BMI ($p<0.001$). Higher TC, TG, LDL-C and VLDL-C levels were observed in obese subjects as compared to controls, except HDL-C, which was significantly lower in obese subjects.

Significant differences ($p<0.05$) were observed in TSH levels in controls as compared to obese subjects. When the TSH levels were correlated among the obese subjects with grade I and grade II obesity according to BMI values, a significant difference ($p<0.05$) in TSH levels were observed, highlighting the variation in TSH levels depending on the extent of obesity.

Conclusion: With the current understanding of patients with thyroid disorders, the lipid profile, BMI and TSH should be well correlated among the subjects presenting with obesity. As the lipid profile is deranged with higher BMI, it imparts resistant to TSH in peripheral tissue further aggravating the thyroid problem. A closer examination of TSH is required in obese subjects, as these subjects are prone to develop cardiovascular diseases.

Key words: Thyroid Stimulating hormone, Lipid Profile, Obesity, BMI, Nepal

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Introduction

Obesity is noticed among all strata of the population in developing countries [1]. It is one of the conventional risk factors for cardiovascular disease (CVD), apart from hypertension, diabetes, hyperlipidaemia and various endocrine disorders [2]. Obesity is defined when the body mass index value exceeds the cut-off value of ≥ 24.9. Obesity is associated with lipoprotein metabolism abnormalities, and its assessment is extremely important in obese subjects, as

they are more likely to develop CVD [3]. With respect to Asians, the criteria of defining obesity in Nepal are different from that of Western countries [4]

Among Asian adults, a BMI value of ≥ 23.0 is considered as obese, as per WHO Experts [5].Hypothyroidism is linked to obesity, and so there must be some link between the thyroid profile and the lipid profile, as derangements of lipid profile are observed in obesity. Even though numerous studies have been conducted earlier to link the thyroid profile parameters, namely thyroid stimulating hormone (TSH), to those with lipid profile, a clear cut relationship between TSH and lipid profile has not been established so far [6],[7]. Latest researchers tried to link thyroid abnormalities with body weight, but the results seem to be normal in euthyroid subjects. Studies showed a positive correlation between TSH levels and BMI (kg/m^2) $\geq$ 40 kg/m^2 [8]. In the European population, a positive correlation has been established between obesity (BMI > 30 kg/m^2) and TSH levels [9]. However, a recent study reported from United Kingdom failed to find a link between these two variables in euthyroid subjects [10]. In context to Nepal, till today, no literature has been reported, focusing on the relationship

between TSH levels and BMI in the Nepalese population. The present study was aimed at the hypothesis of increased TSH levels in obese subjects as compared to controls.

Thus the current study was undertaken to

[1] To establish the correlation between serum TSH levels and varying degrees of obesity, depending on the body mass index (BMI).

[2] To evaluate the relationship between BMI and lipid profile.

Material and Methods

Two hundred and thirty seven subjects including both obese and control subjects, with ages ranging from 30 to 65 years, mean (±SD) 40.56 ± 0.93, were recruited from the Western Regional Hospital, Pokhara, Nepal. Subjects with BMI values $\geq$ 23 kg/m^2 were classified as obese, and those with BMI values $\leq$ 23 kg/m^2 as controls. The obese subjects were further classified into two groups, Obese I (23- 26 kg/m^2) and Obese II ($\geq$ 26 kg/m^2).

Following the above criteria, 183 obese subjects (102 males; 81 females) and 54 controls (29 males; 25 females) were recruited for the study. An informed consent was obtained from the subjects before participating in the study, and the study design was pre-approved by the institutional ethical committee board of Pokhara University, Nepal.

Exclusion criteria: Subjects with known hypercholesterolaemia, hyperthyroidism, diabetes, hypertension, renal failure, cardiovascular disease, cancer and other known diseases.

A pre-tested questionnaire was used to record the age, height, weight, waist circumference (WC), hip circumference (Hp) and waist-to-hip ratio (W/H) . Height was measured in centimeters and weight in kilograms using a calibrated spring balance. Supine waist girth was measured at the level of the umbilicus with a person breathing silently, and standing hip girth was measured at the inter-trochanteric level.

The BMI was calculated by dividing weight (kg) by height (m^2).

Blood pressure and pulse rate of the participants were also recorded. The blood pressure was measured using a standard mercury manometer. At least two readings at 5 minutes intervals, as per the World Health Organization guidelines, were recorded. If high blood pressure (≥140/90 mmHg) was noted, a third reading was taken after 30 minutes. The lowest of the three readings was taken as blood pressure. The measurement of pulse rate was done by feeling the palpitation on the wrist for one minute.

Lipid Profile

Total Cholesterol (TC), Triglyceride (TG) and High-density lipoprotein cholesterol (HDL-C) were analyzed enzymatically using a kit obtained from Randox Laboratories Limited, Crumlin, UK. Plasma LDL-cholesterol (LDL-C) was determined from the values of total cholesterol and HDL-cholesterol using the following formula:

LDL-cholesterol = TC – TG – HDL-cholesterol (mg/dl)

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Other assays- Blood sugar was determined using an enzymatic glucose oxidase peroxidase (GOD-POD) method with deproteinisation, using a Human Diagnostic kit obtained from Germany.

Serum Creatinine was determined by Jaffe's method using a Human kit.

The Serum Urea was determined by the Berthelot reaction based on the hydrolysis of urea to ammonia and carbondioxide. Further, the ammonium ions reacts with hypochlorite and salicylate to form a green dye, and the absorbance was proportional to the concentration of urea.

Serum SGPT was determined using an enzymatic method based on the formation of glutamate and oxaloacetate from α-ketoglutarate and aspartate. The oxaloacetate formed further in the presence of malonate dehydrogenase was converted to malate. The absorbance was based on formation of NAD^+ at 340 nm. TSH was determined by enzyme linked immunosorbent assay (ELISA), using a kit obtained from Ranbaxy Laboratories.

Statistical Analysis

All statistical analyses were performed using the SPSS version 11.0. The data was presented as mean ± Standard error mean. Correlations between measured parameters were assessed using the analytical method of Pearson co-efficient. Comparison of parameters between obese and non-obese subjects was performed by using the Mann-Whitney test and Kruskal-Walis test. P <0.05 was considered to be statistically significant.

Result

The mean and standard error mean (SEM) of age, weight, height, WC, W/H ratio, Systolic blood pressure (SBP) and Diastolic blood pressure (DBP) are presented in [Table/Fig 1]. A significant difference in Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was observed between obese and non-obese subjects (SBP; $p<0.05$; DBP; $p<0.05$). Weight, WC and W/H ratio, significantly, was positively correlated with increasing BMI ($p<0.001$). Systolic and diastolic blood pressure, weight, WC and W/H ratio also positively correlated with BMI (data not shown).

The biochemical parameters of the participants are presented in [Table/Fig 2]. The study observed significantly higher TC, TG, LDL-C and VLDL-C levels in obese subjects as compared to controls, except HDL-C levels which were significantly lower in obese subjects [Table/Fig 2].

The mean TSH levels in controls and obese subjects are presented in [Table/Fig 3]. A significant difference ($p<0.05$) was observed in TSH levels in controls, as compared to the obese subjects. When the TSH levels were correlated among the obese subjects with grade I and grade II obesity, BMI values significantly increased ($p<0.05$) [Table/Fig 4], highlighting the variation in TSH levels depending on the extent of obesity.

(TABLE/Fig 1) Anthropometric variable in Obese and Non- Obese subjects

Parameters	Control (n=54)	Obese (n=183)	P value (95% CI)
Age (years)	40.63 ± 1.33	40.77 ± 0.78	0.087 (40.65-40.80)
Height (mt)	1.56 ± 0.01	1.58 ± 0.09	0.0456 (1.56-1.59)
Weight (kg)	52.21 ± 0.98	69.36 ± 0.87	<0.001 (69.23-69.48)
WC (cms)	75.28 ± 1.48	91.30 ± 0.86	<0.001(91.17-91.42)
Hip circumference (cms)	88.56 ± 0.78	103.75 ± 0.73	<0.001(101.34-104.21)
W/H ratio	0.85 ± 0.01	0.88 ± 0.01	<0.001(0.87-0.88)
SBP(mmHg)	118.39 ± 2.72	124.29 ± 1.39	<0.05(124.09-124.48)
DBP(mmHg)	78.50 ± 1.65	83.76 ± 1.04	<0.05(83.21-83.90)

Values are in mean (± SEM)

(TABLE/Fig 2) Lipid profile and biochemical variable in Control and Obese subjects

Parameters	Control (n=54)	Obese (n=183)	P Value (95% CI)
Total cholesterol (mg/dl)	160.73 ± 4.75	173.97 ± 3.19	<0.01(173.51-174.42)
Triglycerides (mg/dl)	108.59 ± 7.82	162.44 ± 11.94	<0.001(160.75-164.12)
HDL (mg/dl)	41.02 ± 1.52	39.08 ± 1.36	0.0864 (38.88-39.27)
LDL (mg/dl)	95.43 ± 5.18	104.38 ± 4.27	<0.05(103.77-104.98)
VLDL (mg/dl)	22.28 ± 1.56	31.91 ± 2.37	<0.05(31.57-32.24)
Fasting Glucose (mg/dl)	77.71 ± 1.94	80.12 ± 1.67	0.134 (79.88-80.35)
Serum Urea (mg/dl)	26.89 ± 1.19	28.18 ± 1.24	0. 245 (28.00-28.35)
Serum Creatinine (mg/dl)	0.97 ± 0.41	1.02 ± 0.37	0. 324 (0.96-1.07)
SGPT (U/L)	27.45 ± 1.09	30.71 ± 2.45	0. 068 (30.36-31.05)

Values quoted as mean ± SEM

(TABLE /Fig 3)TSH level in Obese and Control subjects

Parameter	Control (n = 54)	Obese (n = 183)	*P* value (95% CI)
Mean TSH(μIU/mL)	2.32 ± 0.23	2.64 ± 0.11	<0.05 (2.62-2.65)

(TABLE/Fig 4)TSH level in Grade I and II Obesity

Parameter	Obese I (n = 79)	Obese II (n = 104)	*P* value (95% CI)
TSH(μIU/mL)	2.62 ± 0.23	2.68 ± 0.13	<0.05 (2.66-2.69)

Discussion

Obesity is a conventional risk factor for cardiovascular disease, and is emerging as a major health problem in developing countries. The relationship between obesity, lipid profile and thyroid dysfunction is a concern for researchers, and studies are being carried out to link up these three aspects. Lipid and thyroid profiles are the most common investigations called for in obese subjects by clinicians, even though data linking obesity and thyroid functions fail to prove a significant relationship between them [11],[12]. Lipid abnormalities have been reported in obese individuals, especially in central obesity [8],[9],[13]. The present study was aimed to examine the relationship between obesity and lipid profile with respect to the Nepalese population who are inhabitantsa of Pokhara Valley, where there a higher trend of obesity has been found among the locals in recent years. The International Obesity Task Force stated that the approach to obesity should be considered on the basis of regional variations. Among Asians, the cut-off value for BMI is 23 kg/m^2, to define obesity, and the classification of obesity is based on BMI values ranging from 22-26 kg/m^2; however, the clear cut demarcation of obesity is based on BMI values more than 26 kg/m^2[14],[15],[16].

In the present study, dyslipidaemia was observed among obese subjects, and significantly higher levels of TC, TG, VLDL-C and LDL-C were observed in obese subjects as compared to the non-obese, which concurs with the reports of the previous studies [3],[17]. The present study observed that only TG levels positively correlated with BMI. Studies conducted elsewhere, reported that an increase in BMI was associated with an increase in TG, and a decrease in HDL-C levels [5] ,[6], [7].

In the current study, a positive correlation was observed between TSH levels and obesity. In addition, TSH levels were significantly higher, with high borderline values of BMI, as compared to the lower BMI values. Similar findings were reported [9] where there was a positive correlation between varying degrees of obesity and varying TSH levels. Earlier studies conducted, also observed an association between BMI and TSH levels, showing varying TSH levels depending on the degree of obesity from mild to severe [8]. The mechanism of elevated TSH levels in obese subjects still remains unclear [11], but increased TSH levels are suggestive of non responding receptors of target cells to TSH , a phenomenon similar to insulin resistance observed in diabetes [18],[19]. This theory has some merit, since T_3 receptors are decreased in obesity, resulting in a relative pituitary resistance to thyroid hormones [20], [21]. A TRH stimulation test (TRH-t) could rule out whether the pituitary response is altered in the obese population (22, 23). It is also postulated that the production of TSH is also regulated by transmitters and hormones that regulate body weight satiation such as neuropeptide Y (alpha), melanocyte stimulating hormones and the agouti-related peptide innervating TRH synthesizing neurons [24],[25]. The other possible mediator of increased TSH secretion could be Leptin, as suggested by earlier reports [11]. The study has its

limitations, as we did not measure serum fT_4 and fT_3 in our subjects, which could have added more information on the status of thyroid function.

The current study did not observe any significant difference between TSH levels and lipid profile pattern, as reported in earlier studies [3],[4]. In obese sub clinical hypothyroid patients, higher energy expenditure is observed with higher TSH levels, but does not alter body composition and lipid profile [26].

The study did not observe significant differences in BMI, body weight, WC, W/H ratio and dyslipidaemia with respect to elevated TSH levels when compared to normal TSH levels, but significant difference in BMI was observed within normal TSH levels.

Furthermore, the study observed elevated TG and lower HDL-C levels to be associated with higher BMI, showing a higher risk of cardiovascular diseases in obesity. A large scale study involving more health personnel and researchers are required to further carry out this work to validate the findings of the current study.

Conclusion

With the current understanding of patients with thyroid disorders, the lipid profile, BMI and TSH should be well correlated among the subjects presenting with obesity. As lipid profile is deranged with higher BMI, which imparts resistant to TSH in peripheral tissue further aggravating the thyroid problem. A closer examination of TSH is required in obese subjects, as these subjects are prone to cardiovascular diseases.

Acknowledgements

The authors express their gratitude towards Pokhara University for granting funds for this project. The authors are also thankful to Mr. Niranjan Shrestha, Lecturer, Biostatistics, School of Pharmaceutical and Biomedical Sciences, Pokhara University for data analysis.

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