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Research Article

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The Relationship between Serum Thyrotrophic and Components of Metabolic Syndrome

Khalid S Aljabri* and Samia A Bokhari

Department of Endocrinology, King Fahad Armed Forces Hospital, Jeddah, Kingdom of Saudi Arabia

***Corresponding author**
Khalid S Aljabri, Department of Endocrinology, King Fahad Armed Forces Hospital, Jeddah, Kingdom of Saudi Arabia, PO Box 9862. Jeddah 21159. Kingdom of Saudi Arabia, Tel: +9662323333; ext. 59200, E-mail: khalidsaljabri@yahoo.com

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Abstract

Background and objective: *Metabolic syndrome (Meets) is a cluster of obesity, hyperglycemia, dyslipidemia and hypertension (HTN). Thyroid hormones play an important role in regulating energy homeostasis, carbohydrate, lipids and protein metabolism. Therefore the present study was an effort to investigate the influence of TSH levels in each component of patients with Meets in a population of Saudi Arabia.*

Design: *We analyzed retrospectively 656 participants with MetS whom are between the ages 20 to 98 years. All patients were from the population of the Primary health centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. All data were collected on the basis of a review of electronic medical data. Patient who are pregnant were excluded. The reference range values of TSH 0.22-4.2 MIU/L, Free T4 12.0-22.0 pmol/L. TSH was divided into three groups; <1.5, 1.5-2.5 and >2.5-4.2. Metabolic risk factors were defined using the 2006 IDF criteria that define elevated triglyceride as ≥150 mg/dL (≥1.7 mmol/L) and reduced high density lipoprotein cholesterol (HDL) as <40 mg/dL (<1.03 mmol/L) for male and as <50 mg/dL (<1.29 mmol/L) for female. Elevated blood pressure was defined when the systolic blood pressure was ≥130 mm Hg and/or diastolic blood pressure was ≥85 mm Hg in addition to receiving any medication for HTN. Abnormal glucose metabolism was con¬sidered when HbA1c (≥5.7) or when patients were known to have type 2 diabetes mellitus (T2DM). The total number of cohort was separated on basis of age values into four groups: <40 years, 40-49 years, 50-59 years and ≥60 years.*

Results: *656 subjects with MetS were included. There were 86 (13.1%) male and 570 (86.9%) were female with mean age 55.6 ±12.7 with mean body mass index 32.8 ± 7.2 kg/m^2. HbA1c>5.6 or T2DM, hypertension, triglyceride (≥1.7 mmol/l) and low HDL were present in 94 (14.3%), 354 (54.0%), 328 (50.2%) and 487 (74.2%) respectively. The mean TSH and FT4 values were 2.1 ±1.0 mIU/l and 15.4 ±3.1 pmol/l respectively. Patients with TSH (>2.5-4.2) were non-significantly younger and have significantly higher BMI compared to patients with TSH (<1.5) or TSH (1.5-2.5), 50.9 ±12.4 vs. 53.5 ±12.7 vs. 53.4 ±13.0 respectively, p=0.05 and 33.6 ± 8.2 vs. 31.7 ± 6.1 vs. 33.2 ± 7.0 respectively, p=0.01. Females compared to males were non-significantly predominant in patients with TSH (>2.5-4.2) compared to patients with TSH (<1.5) or TSH (1.5-2.5), 87.3 vs. 12.7%, 89.4 vs. 10.6% and 84.0 vs. 16.0%, p=0.2. Cases with HbA1c>5.6 or T2DM were significantly more prevalent in patients with TSH (>2.5-4.2) compared to TSH (<1.5) or TSH (1.5-2.5), 18.8% vs. 13.9% vs. 10.0 respectively, p=0.03. Cases with HTN were significantly less prevalent in patients with TSH (>2.5-4.2) compared to TSH (<1.5) or TSH (1.5-2.5), 46.3% vs. 54.3% vs. 61.6 respectively, p=0.005. Cases with serum triglyceride (≥1.7 mmol/l) were significantly more prevalent in patients with TSH (>2.5-4.2) compared to TSH (<1.5) or TSH (1.5-2.5), 57.6% vs. 44.9% vs. 47.2 respectively, p=0.02. Cases with low HDL were significantly more prevalent in patients with TSH (>2.5-4.2) compared to TSH (<1.5) or TSH (1.5-2.5), 85.1% vs. 74.9% vs. 71.1 respectively, p=0.002. Higher prevalence of HbA1c>5.6 or T2DM, low HDL , triglyceride (≥1.7 mmol/l) and HTN in patients with age 40-59 years compared to <40 years or more than 60 years, p<0.0001, p=0.4, p=0.02 and p=0.3 respectively.*

Conclusion: *We found that an increase in serum TSH was positively correlated with components of metabolic syndrome and might be a risk factor for metabolic syndrome in Saudis. Further investigations are essential to further confirm the relationship between TSH and components of metabolic syndrome in Saudis as well as the underlying mechanism(s).*

Keywords: Serum Thyrotrophic, Metabolic Syndrome, Saudi Arabia

Introduction

Metabolic syndrome (MetS) is a cluster of obesity, hyperglycemia, dyslipidemia and hypertension (HTN), which is one of the major

public health issues [1]. The prevalence of MetS in western countries is about 20% to 30%, while it is about 10% to 21% in Saudi Arabia [2-5].

Thyroid hormones play an important role in regulating energy homeostasis, carbohydrate, lipids and protein metabolism. Thyroid functions affect the components of MetS including high density lipoprotein–cholesterol (HDL-C), triglycerides (TG), blood pressure and plasma glucose. There are several studies about the correlation between thyroid function and components of MetS, but the results are disputed. A cross-sectional study of 1581 thyroid subjects found that there was positive correlation between serum thyrotrophic (TSH) and index of insulin resistance as well as TG [6].

Bakkar et al. showed that insulin resistant subjects are more susceptible to the increased levels of high LDL-C at increasing TSH levels even within the normal range [7]. Bauer DC et al showed that among older white women, high TSH levels were associated with deleterious changes in serum lipids and that women with multiple lipid abnormalities were twice as likely to have increased TSH level [8]. The impact of various degree of thyroid dysfunction on components of MetS, however, continues to be debatable [9]. Therefore the present study was an effort to investigate the influence of TSH levels in each component of patients with MetS in a population of Saudi Arabia.

Methods

We analyzed retrospectively 656 participants with MetS whom are between the ages 20 to 98 years. All patients were from the population of the Primary health centre at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. All data were collected on the basis of a review of electronic medical data. Patient who are pregnant were excluded. The reference range values of TSH 0.22-4.2 MIU/L, Free T4 12.0-22.0 pmol/L. TSH was divided into three groups; <1.5, 1.5-2.5 and >2.5-4.2. Metabolic risk factors were defined using the 2006 IDF criteria that define elevated triglyceride as ≥150 mg/dL (≥1.7 mmol/L) and reduced high density lipoprotein cholesterol (HDL) as <40 mg/dL (<1.03 mmol/L) for male and as <50 mg/dL (<1.29 mmol/L) for female. 9 Elevated blood pressure was defined when the systolic blood pressure was ≥130 mm Hg and/or diastolic blood pressure was ≥85 mm Hg in addition to receiving any medication for HTN. Abnormal glucose metabolism was con¬sidered when HbA1c (≥5.7) or when patients were known to have type 2 diabetes mellitus (T2DM). The total numbers of cohort were separated on basis of age values into four groups: <40 years, 40-49 years, 50-59 years and ≥60 years.

Statistical Analysis

Continuous variables were described using means and Standard Deviations. Univar ate analysis of baseline demography both between groups, were accomplished using unpaired t-test and nonparametric and Chi square test were used for categorical data comparison. P value <0.05 indicates significance. The statistical analysis was conducted with SPSS version 23.0 for Windows.

Results

656 subjects with MetS were included. There were 86 (13.1%) male and 570 (86.9%) were female with mean age 55.6 ±12.7 with mean body mass index 32.8 ± 7.2 kg/m2, (Table 1). HbA1c>5.6 or T2DM, hypertension, triglyceride (≥1.7 mmol/l) and low HDL were present in 94 (14.3%), 354 (54.0%), 328 (50.2%) and 487 (74.2%) respectively. The mean TSH and FT4 values were 2.1 ±1.0 mIU/l and 15.4 ±3.1 pmol/l respectively. Patients with TSH (>2.5-4.2) were non-significantly younger and have significantly higher BMI compared to patients with TSH (<1.5) or TSH (1.5-2.5), 50.9 ±12.4 vs. 53.5 ±12.7 vs. 53.4 ±13.0 respectively, p=0.05 and 33.6 ± 8.2 vs. 31.7 ± 6.1 vs. 33.2 ± 7.0 respectively, p=0.01. Females compared to males were non-significantly predominant in patients with TSH (>2.5-4.2) compared to patients with TSH (<1.5) or TSH (1.5-2.5), 87.3 vs. 12.7%, 89.4 vs. 10.6% and 84.0 vs. 16.0%, p=0.2, table 1. Cases with HbA1c>5.6 or T2DM were significantly more prevalent in patients with TSH (>2.5-4.2) compared to TSH (<1.5) or TSH (1.5-2.5), 18.8% vs. 13.9% vs. 10.0 respectively, p=0.03. Cases with HTN were significantly less prevalent in patients with TSH (>2.5-4.2) compared to TSH (<1.5) or TSH (1.5-2.5), 46.3% vs. 54.3% vs. 61.6 respectively, p=0.005. Cases with serum triglyceride (≥1.7 mmol/l) were significantly more prevalent in patients with TSH (>2.5-4.2) compared to TSH (<1.5) or TSH (1.5-2.5), 57.6% vs. 44.9% vs. 47.2 respectively, p=0.02. Cases with low HDL were significantly more prevalent in patients with TSH (>2.5-4.2) compared to TSH (<1.5) or TSH (1.5-2.5), 85.1% vs. 74.9% vs. 71.1 respectively, p=0.002.

Table 1: Base line characteristics and bivariate analysis for hypothyroidism in patients with metabolic syndrome [mean±standard deviation or number (%)]

Parameters		Total	Thyroid stimulating hormone			P value
			<1.5	1.5-2.5	> 2.5-4.2	
Numbers		656	219 (33.4)	208 (31.7)	229 (34.9)	
Age (years)		55.6 ±12.7	53.5 ±12.7	53.4 ±13.0	50.9 ±12.4	0.05
Gender	Male	86 (13.1)	35 (16.0)	22 (10.6)	29 (12.7)	0.2
	Female	570 (86.9)	184 (84.0)	186 (89.4)	200 (87.3)	
Body mass index (kg/m²)		32.8 ± 7.2	31.7 ± 6.1	33.2 ± 7.0	33.6 ± 8.2	0.01
HbA1c>5.6 or Type 2 diabetes		94 (14.3)	22 (10.0)	29 (13.9)	43 (18.8)	0.03
Hypertension		354 (54.0)	135 (61.6)	113 (54.3)	106 (46.3)	0.005
Triglyceride (≥1.7 mmol/l)		328 (50.2)	103 (47.2)	93 (44.9)	132 (57.6)	0.02
High density lipoprotein (<1.29 mmol/l)		487 (74.2)	150 (71.1)	149 (74.9)	188 (85.1)	0.002
TSH (mIU/l)		2.1 ±1.0	1.1 ±0.4	2.1 ±0.3	3.2 ±0.4	<0.0001
FT4 (pmol/l)		15.4 ±3.1	16.2 ±3.6	15.1 ±2.5	14.9 ±3.0	0.003

Higher prevalence of HbA1c>5.6 or T2DM, low HDL , triglyceride (≥1.7 mmol/l) and HTN in patients with age 40-59 years compared to <40 years or more than 60 years, p<0.0001, p=0.4, p=0.02 and p=0.3 respectively (Figure 1 A-D).

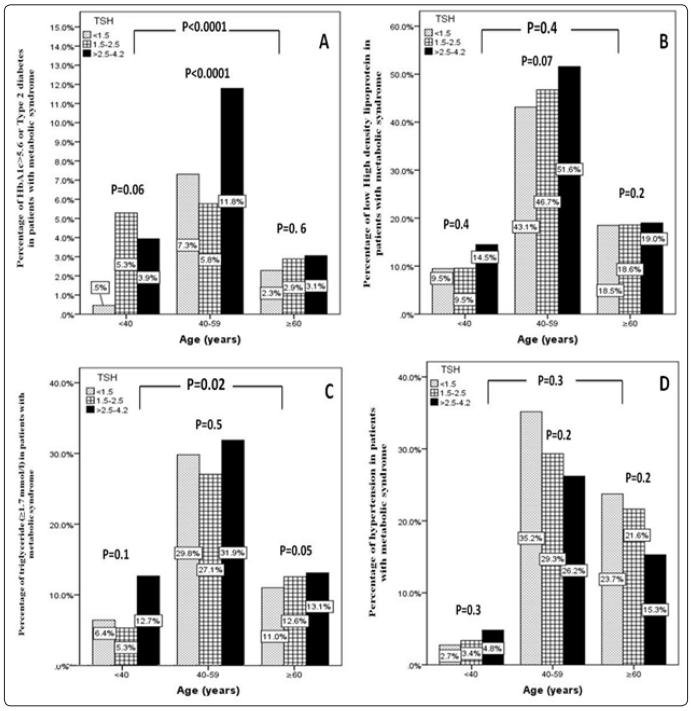

Figure 1 A-D: Percentage of HbA1c>5.6 or type 2 diabetes (A), high density lipoprotein (male <1.03 mmol/l and female <1.29 mmol/l) (B), triglyceride (≥1.7 mmol/l) (C) and hypertension (D) in patients with metabolic syndrome

Discussion

We found that an increase in serum TSH was positively associated with components of MetS and might be a risk factor for MetS in Saudis. MetS can be associated with endocrine and non-endocrine disorders and has widespread consequences. Alterations in thyroid functions, though well known, are not recognized clinically and there is inconsistency in thyroid functions in MetS [10]. A positive association has also been reported, between a higher TSH level within the thyroid reference range and the prevalence of the MetS [11]. A study in Korea indicated that higher levels of TSH may predict the MetS in the study subjects, suggesting that the influence of thyroid function on metabolic abnormality extends into subjects without MetS [12]. Even high normal TSH levels and low normal free T4 levels were significantly associated with increased prevalence of MetS, which may be of importance when evaluating such subjects [6,13].

MetS incidence increases with age as the prevalence of obesity, HTN, dyslipidemia and hyperglycemia also increases during this time [14]. Data regarding gender effect are conflicting with the majority of the studies finding the highest prevalence in women, while the collaborative European analysis found no gender difference [6,14].

Multiple studies in the general population have confirmed positive associations between serum TSH and BMI, HTN and triglyceride levels [13,15-19]. We found that obesity increased the relative risk of thyroid dysfunction in patients with MetS than those with overweight; supporting the results of Biondi et al. who reported a positive correlation between serum lepton and serum TSH levels in obese individuals, which could reflect the positive association between TSH and BMI [20]. The current study showed significantly that higher BMI with associated with upper normal TSH. Some studies suggesting that some humoral or hormonal mediators from adipose tissue stimulate the hypothalamus–pituitary–thyroid axis to increase TSH secretion. The main suspected mechanism is a possible relationship between leptin and the thyroid hormones. There is possibly a relationship between leptin and the thyroid hormones via an influence of leptin on the negative feedback regulation of thyroid hormones. Leptin regulates TRH expression [21]. There are several postulated causes of increased TSH levels in obesity, including autoimmune status, leptin levels, and inflammatory factors. The most favored hypothesis attributes the elevated TSH levels in obesity to increased leptin-mediated production of parathyroid releasing hormone [22].

Our study showed an association between upper normal TSH and higher prevalence of HbA1c>5.6. Some studies described decreased insulin sensitivity in hypothyroidism, while others did not [23-25]. The study of Jackson et al. Teven reported increased insulin sensitivity [26]. Recently, an experimental study in an animal model has demonstrated that the mutation in the a-isoform of the thyroid hormone receptor caused insulin resistance and thyroid hormone resistance [27]. In addition, studies investigating thyroid hormone receptors in MetS subjects (mostly in obese individuals) demonstrated a decrease of thyroid hormone receptor density [28,29].

We also found a significant negative association between upper normal TSH and HTN in discordance with other [30]. Others demonstrated positive and linear correlations between normal range TSH and HTN, whereas other researchers could not confirm these findings [6, 31]. The underlying mechanisms for the relationship between TSH and blood pressure are not fully understood, and further studies are needed.

Thyroid hormones influence various metabolic pathways, and both the composition and transport of lipoproteins are impaired in thyroid diseases. In our current study, an association also was found between elevated TSH and dyslipidemia. Among patients with upper normal TSH levels, hypertriglyceridemia was higher than in participants with normal triglyceride levels. The above findings illustrate the positive relationship between TSH and triglyceride. For HDL-C, the risk of low HDL-C in the low-normal TSH group was less than that in the mid-range TSH or upper normal TSG group which indicated that a decrease in TSH within the normal range could reduce the risk of low levels of HDL-C [30].

In summary, we found that an increase in serum TSH was positively correlated with components of metabolic syndrome and might be a risk factor for metabolic syndrome in Saudis. Further investigations are essential to further confirm the relationship between TSH and components of metabolic syndrome in Saudis as well as the underlying mechanism(s).

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