



STUDY OF ASSOCIATION BETWEEN SUBCLINICAL HYPOTHYROIDISM AND METABOLIC SYNDROME IN OBESE MIDDLE AGED WOMEN



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Abstract

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OBJECTIVES: To study the association of Subclinical Hypothyroidism (SCH) with Metabolic Syndrome (MetS). **MATERIAL AND METHODS:** Thirty obese women with waist circumference more than 80cms and thirty women as controls were included. Vital data including age, waist circumference and blood pressure were noted for both cases and controls. Cases and control groups were compared in terms of lipid profile parameters including fasting blood glucose, total cholesterol, triglycerides, HDL-Cholesterol, LDL- Cholesterol, VLDL-Cholesterol and Thyroid profile parameters including Thyrotropin (TSH), Triiodothyronine (T3), Tetraiodothyronine (T4). **RESULTS:** SCH is known to be associated with increased Blood Pressure, and LDL-Cholesterol, Triglyceride levels and decreased HDL-Cholesterol levels. As expected, the present study found higher levels of Blood pressure, LDL-Cholesterol and Total Triglycerides and lower level of HDL-Cholesterol among test group compared to control group. **CONCLUSIONS:** We observed that serum TSH levels were higher in obese and they were associated with decreased HDL-C levels and increased triglycerides. Therefore thyroid dysfunction is associated with MetS.

INTRODUCTION

The metabolic syndrome (MetS) is associated with multiple cardiovascular risk factors. Insulin resistance is considered as the central pathological link among these risk factors¹.

SCH is a more common disorder than overt hypothyroidism with a prevalence of 1.4–7.8% in older populations and even greater percentiles among women^{2,3}.

Overt Hypothyroidism is associated with Cardiovascular Disease (CVD)⁴. Insulin resistance in Type 2 Diabetes Mellitus (T2DM) is commonly associated with overt hypothyroidism and currently several studies support that, this association also exists in Subclinical hypothyroidism (SCH)⁵.

MetS is a proved risk factor for CVD, SCH is also associated with CVD⁵. There are several studies supporting MetS and its related components are associated with overt hypothyroidism but coming to SCH, only some studies support this association^{5,6,7}.

The pathophysiological basis underlying glucose intolerance, dyslipidemia, abdominal obesity and hypertension has been attributed to insulin resistance and it

was found that insulin resistance modifies the relationship between levels of TSH and Low Density Lipoprotein Cholesterol (LDL-C)⁸.

Hence, the current study is aimed to investigate the relationship between SCH and components of Metabolic Syndrome (MetS).

MATERIALS AND METHODS

The present study was conducted at Department of Biochemistry, Guntur Medical College and Hospital, Guntur during June 2010 and June 2011 with control and test groups.

Control Group (Without Central Obesity):

Females with waist circumference less than 80cm and without any prior history of diabetes, hypertension or any other clinical abnormality were selected as controls.

Test Group (With Central Obesity):

Females with waist circumference more than 80cm and without any prior history of diabetes, hypertension or any other clinical abnormality were included in the Test group.

For both control and test groups the following data was recorded:

1. **Physical Parameters:** a) Blood Pressure- Systolic (SBP) & Diastolic (DBP)

b) Waist Circumference (WC).

2. **Chemical parameters:** Blood samples were collected for the analysis of following;

a) Fasting Plasma Glucose (FPG) by Glucose Oxidase method

b) Lipid profile including Total Triglycerides (TTG) by enzymatic method glycerol phosphate oxidase (GPO), Total Cholesterol, (TCH) by cholesterol oxidase (CHOD-PAP) method, HDL Cholesterol (HDL-C)

c) Thyroid profile: Thyrotropin(TSH), Triiodothyronine(T₃) and Thyroxine (T₄) parameters are measured using ChemiLuminescence Immuno Assay method (CLIA).

RESULTS

The results in the present study show an increase in all the metabolic syndrome parameters among test group except HDLC, where a decrease in HDLC was noted.

Thyroid parameters showed an increase in TSH but T₄ and T₃ were remained same in both control and test groups. The results show the test group subjects comes under SCH

DISCUSSION

Metabolic Syndrome is a cluster of cardio-metabolic risk factors⁹. It is known that cardiovascular system is very sensitive to thyroid function^{10, 11}. SCH is a common condition in obese population³ and is known to be more common among female population^{3, 12, 13}.

In this study significant prevalence of SCH in females with abdominal obesity was noted; with similar observations in studies by Uzunlulu et al¹² and Ghanshyam PS Shantha et al¹³.

Blood pressure

In MetS, the blood pressure elevation is by the activation of the sympathetic nervous system and renin-angiotensin-aldosterone system (RAAS) with consequential sodium retention and volume expansion^{14, 15, 16}. In the current study significant elevation of both systolic and diastolic blood pressure values were noted in the females of test group when compared to the control group.

Lipid abnormalities:

In the present study, test groups showed altered lipid profile parameters i.e. increased levels of Total Triglycerides, Total Cholesterol, LDL-C and decreased levels of

HDL-C. Similarly, higher normal values of Fasting plasma glucose were observed among test group females. All these parameters are risk factors for CVD.

In the liver of insulin resistant individuals, Free Fatty Acid flux is high, triglyceride synthesis and storage is increased and excess triglyceride is secreted as VLDL¹⁷. It is believed that the dyslipidemia associated with insulin resistance is a direct consequence of increased VLDL secretion by the liver¹⁸. Hypertriglyceridemia is commonly associated with reductions in HDL-C. This in part relates to the transfer of triglycerides instead of cholesteryl ester from the core of triglyceride- rich lipoproteins like VLDL and/or LDL to HDL, a process catalyzed by cholesteryl ester transfer protein (CETP)^{19, 20, 21}. This generates a smaller, triglyceride- rich HDL which is a better substrate for hepatic lipase for rapid clearance by the Liver²².

In the setting of hypertriglyceridemia, LDL particles are small and dense as they are triglyceride enriched. Evidence supports an association of small dense LDL with Insulin Resistance which leads to CVD^{23, 24}. Of interest, the MetS has been associated with

increased CETP mass that results in reduced LDL particle diameter in addition to reduced HDL²⁵.

Thyroid abnormalities

Associations among serum TSH and MetS parameters:

In this present study an association of increased TSH with MetS was observed, and this was consistent with abdominal obesity and dyslipidemia that includes higher TG and lower HDL-C. Elevated TSH levels were significantly associated with increased triglyceride levels. Increased levels of TSH were also strongly associated in all individuals with decreased HDL-C (both cases and controls). These findings might implicate that subjects with SCH were also at increased cardiovascular risk.

Elevated TSH is associated with MetS and it is strongly associated with decreased HDL-C²⁶⁻²⁹. The most consistently reported finding is that the serum levels of TSH are higher in obese patients than in healthy controls³⁰⁻³⁴. Some studies have shown that elevated TSH levels are significantly associated with MetS and its components³²⁻³⁷.

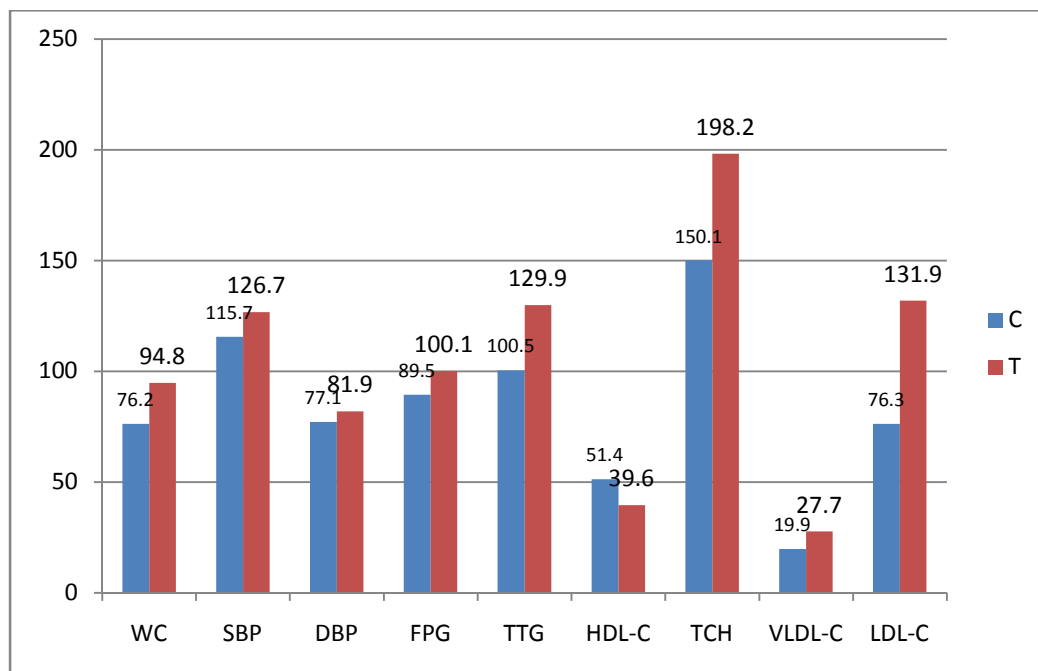
Rondeau *et al*³⁸ found that TSH was negatively correlated with HDL-C in euthyroid obese women. Bakker *et al*³⁹ and The Fremantle Diabetes Study⁴⁰ demonstrated interactions between insulin resistance and thyroid function in euthyroid nondiabetic adults. Their observations reflect the association of insulin resistance with low serum HDL-C and increased TGs⁴¹.

HDL cholesterol along with its constituent apoprotein A1 are well known^{42,43}.

We observed that serum TSH levels were higher in obese and they were associated with decreased HDL-C levels and increased triglycerides. The association between HDL-C and TSH exists irrespective of obesity. Therefore thyroid dysfunction is associated with MetS.

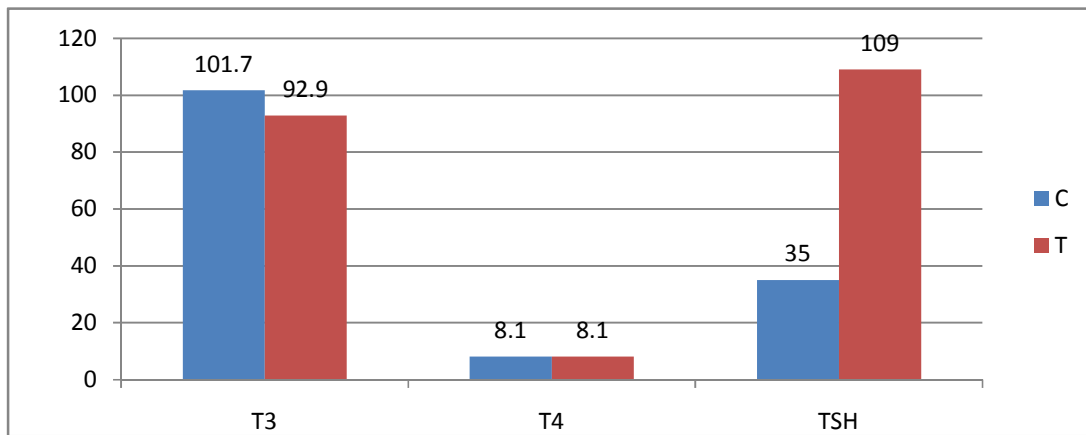
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GRAPH 1 SHOWING METABOLIC SYNDROME PARAMETERS



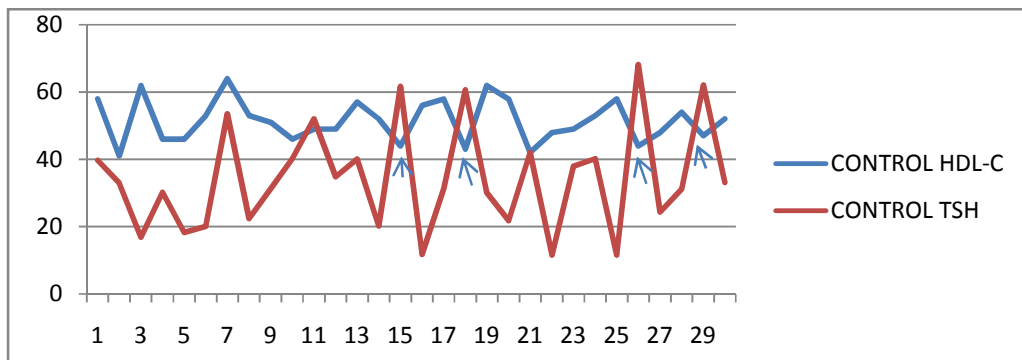
C-Control group T-Test group

GRAPH 2 SHOWING THYROID PROFILE PARAMETERS

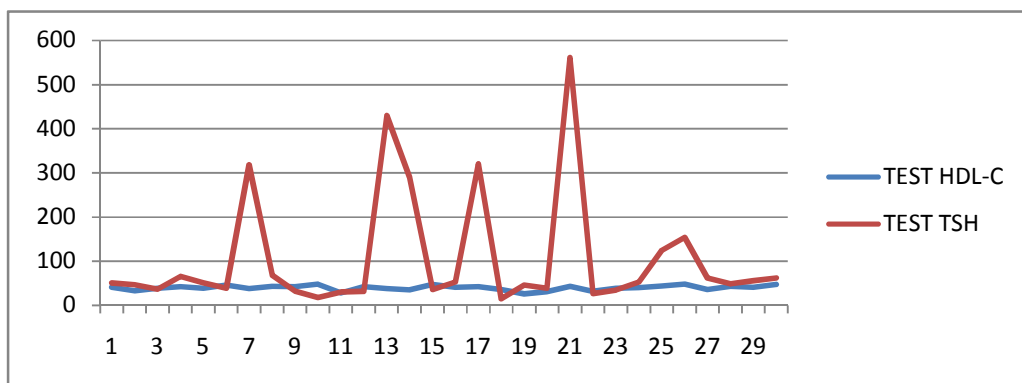


C-Control group T-Test group

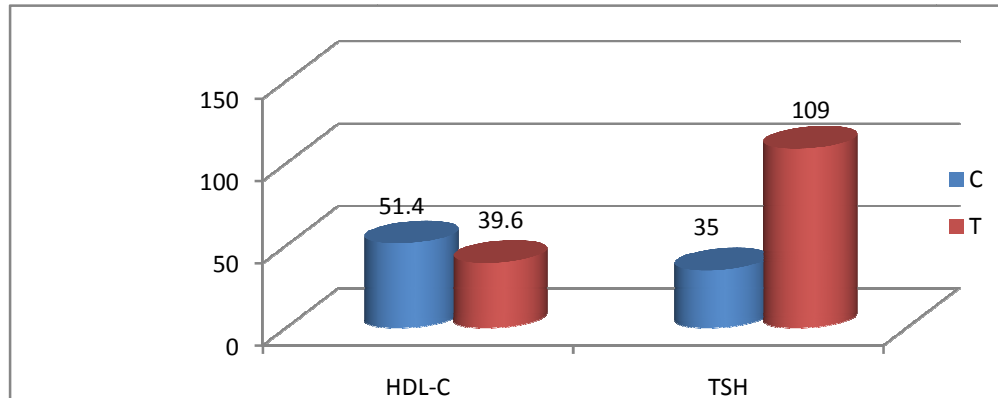
GRAPH 3 Comparison of TSH and HDLC in controls (TSH levels expressed in mIU/dl):



GRAPH 4 Comparison of TSH and HDLC in Test group (TSH levels expressed in mIU/dl)



GRAPH 5 Comparison of TSH and HDLC in Test and Control group (TSH levels expressed in mIU/dl)



C = Control; T = Test

Table 1
SHOWING SIGNIFICANCE OF METABOLIC SYNDROME PARAMETERS

Name of the parameter		Mean ±SD	pvalue	Significance
Systolic blood pressure	Case	126.7±8.13	<0.001	Highly significant
	Control	115.7± 8.13		
Diastolic blood pressure	Case	81.9±6.34	<0.01	significant
	Control	77.1±6.12		
Fasting plasma glucose	Case	100.1±19.7	<0.01	significant
	Control	89.5±6.04		
Total triglycerides	Case	129.9±51.8	<0.01	significant
	control	100.5±23.1		
HDL-C	Case	39.6±5.64	<0.001	Highly significant
	Control	51.4 ±6.3		

Table 2
SHOWING SIGNIFICANCE OF THYROID PROFILE

Thyroid parameter		Mean ± SD	pvalue	Significance
T ₃	Case	93.00± 30.00	<0.5	Not significant
	Control	102.00± 25.80		
T ₄	Case	8.07±2.25	-	-
	Control	8.08±1.74		
TSH	Case	8.15±7.60	<0.02	significant
	Control	3.60±1.85		

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