Thyrotropin and Free Thyroxine Levels in Industrial Workers with Metabolic Syndrome in Port Harcourt

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Abstract
Background: *Metabolic syndrome and hypothyroidism are independent risk factors for cardiovascular disease. The prevalence of each is rising exponentially. It is possible that patients with both disease entities may have a compounded risk especially considering the association of metabolic syndrome with plasma glucose levels and the intricate relationship between plasma glucose and thyroid function.*
Objective: *The objective of this study is to examine the possible association between metabolic syndrome and thyroid function in industrial workers.*
Patients and Methods: *A total of 93 subjects were recruited for this study. 48 had metabolic syndrome (using NCEP ATP III criteria) and formed the study group while 45 age- matched subjects were recruited into the control group. Basic demographic data, components of the metabolic syndrome, thyrotropin and free thyroxine were estimated for all subjects using standard methods. Appropriate statistics were used to analyze data.*
Results: *Components of the metabolic syndrome and thyrotropin were significantly higher in the study group (P<0.05) while high density lipoprotein cholesterol and free thyroxine were significantly lower in the study group (P<0.05). 42 (87.5%) of the study group and 8 (18%) of the control group had sub-clinical hypothyroidism (high thyrotropin with normal free thyroxine (P<0.05). Women with metabolic syndrome are more associated with sub-clinical hypothyroidism (P=0.025) CI: 1.950-13.212).*
Conclusion: *Sub-clinical hypothyroidism is significantly associated with metabolic syndrome in industrial workers. Females have an increased risk of this association. There may be an increased risk for cardiovascular disease and need for thyroid replacement therapy for this group of patients.*

Keywords: Metabolic syndrome, Thyrotropin, Free-thyroxine, sub-clinical hypothyroidism.

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Introduction

Metabolic syndrome is increasingly assuming epidemic proportion in most populations of the world with a rising incidence of insulin resistance.[1,2] It is predicted that metabolic syndrome may eventually bankrupt the health system. Metabolic syndrome is defined by the presence of three or more of the following criteria in an individual:[3,4]

Blood pressure (mmHg) e" 130/85

Fasting plasma glucose e" 110mg/dl (6.1mmol/l)

Triglyceride > 150mg/dl (1.70mmol/l)

High density lipoprotein cholesterol < 40mg/dl (1.0mmol/l) in men and <50mg/dl (1.3mmol/l) in women

Waist circumference > 40 inches (102cm) in men and 35 inches (88cm) in women).

Individuals with this syndrome have pro-inflammatory and pro-thrombotic tendencies. The central activating mechanism in this syndrome is insulin resistance.[2,5] Both metabolic syndrome and insulin resistance are risk factors for cardiovascular disease and diabetes, two of the leading causes of death in the world today.[1,2,5] Several clinical syndromes have also been associated with insulin resistance.

There is a rising prevalence of hypothyroidism affecting a sizeable proportion of different populations.[6-9] Thyroid disease (hypothyroidism) is associated with cardiovascular disease.[8,9] As metabolic syndrome and hypothyroidism are independent risk factors for the same disease process, namely cardiovascular disease, it is possible that patients with the two disease entities may have a compounded risk, particularly when one considers the fact that you need a sustained normal plasma glucose to maintain proper thyroid function and sustaining normal plasma glucose requires a proper functioning thyroid gland.[8-10] In metabolic syndrome, there is impaired plasma cholesterol.[3] There is however scanty data on the prevalence of sub-clinical hypothyroidism in Nigeria.

Thyrotropin (TSH) is the most common test for screening for thyroid dysfunction.[11-13] In the last decade, the diagnostic strategy for using TSH measurements has changed as a result of the sensitivity improvements in these assays. It is now known that TSH measurements is a more sensitive test than thyroxine (T_4) for detecting both hypo-and hyperthyroidism.[13] However, while a measure of TSH alone is a useful screening tool in assessing thyroid function, including free thyroxine (T_4) provides a more complete evaluation of the thyroid.[13-15] It has become evident that many cardiovascular risk factors tend to cluster around metabolic syndrome, it could be hypothesized that thyroid is associated with metabolic syndrome.

The aim of our study is to investigate the levels of TSH and free T_4 in individuals that satisfy the criteria for metabolic syndrome and thus examine the relationship between metabolic syndrome and thyroid function in industrial workers who because of their life style tend to be relatively more obese.

Patients and Methods

A total of forty eight (48) patients with metabolic syndrome formed the study population for this study. A total of forty (40) subjects were recruited to form the control group. Both study and control groups were aged between 30 and 65 years. Study population subjects were selected serially from the patients attending the obesity/metabolic specialist clinic of the NNPC Eastern zonal hospital at Waterlines Port Harcourt; while the control group subjects were recruited from industrial workers who came for routine medical examinations at the general out-patient department of the same hospital. Standard criteria for metabolic syndrome (according to NCEP ATP III)[3] was used.

This study lasted a period of one year and six months (from February, 2010 to August, 2011). Out of the 48 patients with metabolic syndrome, 32 (67%) were women while 16 (33%) were men. Of the 45 subjects in the control group, 30(67%) were women while 15 (33%) were men. Subjects with clinical hypothyroidism, clinical hyperthyroidism, frank diabetes, liver disorders, renal disorders, congestive cardiac failure as well as smokers, alchoholics and pregnant women were excluded from this study. Also excluded were subjects on the following drugs: anti-thyroid, thyroid replacement, drugs that alter thyroid function, oral contraceptive pills, and drugs that alter lipid levels.

Baseline demographic data was collected from both study and control groups and detailed physical examination carried out. Blood pressure was measured using a mercury sphygmomanometer (ACCOSON). The blood pressure (in mmHg) was measured over the right arm with the patient lying supine. Three readings were taken and a mean value taken as the final reading for each subject. Waist circumference was measured at the plane between the anterior superior iliac spines and lower coastal margin at the narrowest part of the waistline while the subject was standing and during expiration. Fasting blood specimens were obtained from all the subjects (venous blood). This was after overnight fast of a minimum of eight hours. This fasting blood specimen was used for the estimation of plasma glucose, total cholesterol, high density lipoprotein cholesterol and triglyceride. Total cholesterol was determined using enzymatic method.[16] High density lipoprotein cholesterol was determined by precipitation method.[17]

Triglyceride and plasma glucose were determined by enzymatic method.[18,19] Low density lipoprotein cholesterol was calculated using the Friedwald's formular.[21] Serum TSH and free T_4 measurements were made using Roche elecsys modular analytics E170 using electrochemiluminescence immunoassay (ECLIA method).[13-15] Using this method, the normal range for TSH was 0.27-0.42μiu/ml and for normal free thyroxine (FT_4) was 0.93-1.7ng/dl; a high TSH (between 4.2-10μiu/ml) and a normal free T_4 are required to classify an individual as having subclinical hypothyroidism.[13,21-24] Informed consent was obtained from all the study participants and the hospital management committee (which also functions as the ethics committee) approved the study. Baseline characteristics of the study and control groups are expressed as mean (standard deviation) and percentage. Student's't' test was used to analyze baseline characteristics between the study and control groups.

Chi-square test was used to analyze the association between metabolic syndrome and thyroid function (expressed by TSH and FT_4). Association between patients characteristics (gender, age, mean systolic BP, mean Diastolic BP, waist circumference, total cholesterol, triglyceride, fasting plasma glucose, high density lipoprotein cholesterol and low density lipoprotein cholesterol) and thyroid function (TSH and FT_4) in the study group were analyzed using multiple logistic regression. P-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS windows version 16.0 software.

Results

48 patients formed the study group and of these, 32 were women (67%) and 16 were men (33%) with mean age of 41(5.2) years. The control group (n=45) had 30 women (67%) and 15 men (33%) with mean age of 42 (6.3) years. The baseline characteristics of the two groups are shown in (Table 1). From the table, the two groups were similar with respect to sex and age ($P>0.05$). However, mean waist circumference, systolic blood pressure, diastolic blood pressure, total cholesterol, triglyceride, fasting plasma glucose, low density lipoprotein cholesterol and thyrotropin (TSH) were significantly higher in the study group compared to the control group ($P<0.05$). High density lipoprotein cholesterol and free thyroxine values are significantly lower in the

study group compared to the control group (P<0.05).

Table 2 shows the proportion of study and control groups that had overt hypothyroidism, sub-clinical hypothyroidism, Euthyroid state

Table 1. Study group characteristics compared with that of the control group

Parameters	Study Group (Met.Syn Group) (n=48)	Control group (n=45)	P-Value
Men	16 (33%)	15 (33%)	0.66
Women	32 (67%)	30 (67%)	
Age	41 (5.2)	42 (6.3)	0.59
Waist circumference	103 (3.66)	81.7 (5.1)	0.002
Systolic BP (MMHg)	139.2 (4.8)	122.4 (2.7)	0.001
Diastolic BP (MMHg)	90.5 (6.1)	83.3 (2.2)	0.001
TC (mmol/l)	5.7 (0.7)	4.6 (0.8)	0.015
TG (mmol/l)	1.85 (0.4)	1.28 (0.6)	0.001
FPG (mmol/l)	6.5 (0.6)	4.9 (0.5)	0.029
HDL-C (mmol/l)	0.8 (0.2)	1.2 (0.1)	0.030
LDL-C (mmol/l)	3.4 (0.6)	2.7 (0.5)	0.025
TSH (μiu/ml)	5.8 (3.7)	3.7 (3.2)	0.026
FT_4 (ng/dl)	1.09 (0.5)	1.38 (0.7)	0.038

Key: *Met.Syn = Metabolic syndrome*
BP = Blood pressure; TC – total cholesterol
FPG = Fasting plasma glucose; TG – Triglyceride
HDL-C = High density lipoprotein cholesterol
LDC-C = Low density lipoprotein cholesterol
TSH = Thyroid stimulating hormone (Thyrotropin)
FT_4 = Free Thyroxine

Table 2: Thyroid function (TSH & FT_4) in the study and control groups

Thyroid State	Study Group (Met.Syn Group) (n=48)	Control Group (n=45)	P - Value
Overt Hypothyroidism (High TSH + Low FT_4)	0 (0%)	0 (0%)	
Sub-clinical Hypothyroidism (High TSH + Low-Normal FT_4)	42 (87.5%)	8 (18%)	0.0001
Euthyroid (Normal TSH + Normal FT_4)	6 (12.5%)	37(82%)	0.0001
Hyperthyroidism (Low TSH + High FT_4)	0 (%)	0 (%)	

and hyperthyroidism. From this table, 42 (87.5%) of the study group and 8 (18%) of the control group had sub-clinical hypothyroidism (High TSH + Normal FT_4) and this difference was statistically significant (P<0.05). Also, 6 (12.5%) of the study group and 37 (82%) of the control group are Euthyroid (Normal TSH + Normal T_4); this difference was statistically significant (P<0.05). None of the subjects in the study and control groups had overt hypothyroidism (High TSH + Low FT_4) or hyperthyroidism (Low TSH + High FT_4).

Table 3: Association between patient characteristics and sub-clinical hypothyroidism in the study (met.syn) group using multiple regression analysis

Parameters	Odds Ratio	Confidence Internal	P-Value
Age	0.401	0.421-1.102	0.234
Gender	7.521	1.950-13.212	0.025
Systolic BP	0.651	0.540-1.320	0.087
Diastolic BP	0.288	0.280-2.988	0.250
Waist circumference	2.110	0.590-1.920	0.320
TC	1.520	1.620-1.949	0.318
TG	0.200	0.150-1.124	0.071
HDL-C	1.301	0.521-3.994	0.421
FPG	0.298	0.650-2.501	0.385

Table 3 shows the association between patient characteristics and sub-clinical hypothyroidism in the study (metabolic syndrome) group using multiple regression analysis. Logistic regression analysis recognized the association between female gender (P=0.025, CI: 1.950-13.212) and sub-clinical hypothyroidism.

Discussion

In our study, mean systolic blood pressure, diastolic blood pressure, waist circumference, fasting plasma glucose, triglycerides and thyrotropin values were significantly higher in the metabolic syndrome group (study group) compared to the control group. High density lipoprotein cholesterol and free thyroxine were significantly lower in the metabolic syndrome group (study group) compared to the control group. Sub-clinical hypothyroidism was found to be significantly more associated with the metabolic syndrome (study) group than with the control group. This association is quite strong.

Similar to our observation in this study, studies by GP Shantha *et al*.[20] and Uzunlulu M, *et al*[23] had shown prevalence of sub-clinical hypothyroidism in metabolic syndrome patient to be 21.9% and 16.4% respectively. The percentage of sub-clinical hypothyroidism observed in our study is quite higher (87.5%) than in the previous studies although our study population is different from those of the other studies and is relatively smaller as we concentrated only on industrial workers.

Supporting the findings in our study, thyroid function has consistently been associated with individual components of the metabolic syndrome. Recent studies have established the association between free thyroxine levels and total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglyceride.[12,20,24] Another study had shown the association between sub-clinical hypothyroidism and increased levels of lipoprotein (a).[25] With regard to other components of the metabolic syndrome, it had also been reported that a low normal free thyroxine level was significantly associated with insulin resistance and sub-clinical hypothyroidism has been associated with fasting hyperinsulinaemia.[12,19]

From the foregoing, hypothyroidism is significantly associated with every individual component of the metabolic syndrome. In our study, females with metabolic syndrome had significant association with sub-clinical hypothyroidism. This agrees with the findings from other studies.[20,23]

Conclusion

Sub-clinical hypothyroidism is significantly associated with metabolic syndrome in our environment. Females have an increased risk of this association. It is advisable to screen metabolic syndrome patients (especially females) for sub-clinical hypothyroidism. High TSH and low normal free T_4 are risk factors for metabolic syndrome in this environment. It might be necessary to carry out further studies on the role of thyroxine replacement therapy in metabolic syndrome patients with sub-clinical hypothyroidism. Whether the duo of metabolic syndrome and sub-clinical hypothyroidism will result in a compounded risk of cardiovascular disease will be a subject of further studies.

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