

CORRELATION BETWEEN METABOLIC SYNDROME AND SUBCLINICAL HYPOTHYROIDISM IN PATIENTS PRESENTING TO OPDS OF PAF HOSPITAL ISLAMABAD

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Abstract:

Background: Subclinical hypothyroidism (SCH), marked by elevated levels of thyroid-stimulating hormone (TSH) has a strong bearing upon on metabolic processes and exploring a correlation of SCH and metabolic syndrome (MetS) would be useful in management of metabolic related disorders especially among the cardiac patients.

Objective: To determine the correlation between metabolic syndrome and subclinical hypothyroidism in patients presenting to OPDs of PAF Hospital Islamabad.

Material and Methods: This case control study was conducted at the Department of Medicine, PAF Hospital Islamabad, Pakistan from 1st of March 2023 to 31st of August 2023. Total numbers of 278 patients with metabolic syndrome were enrolled in study group while another 278 healthy individuals not having features of MetS were enrolled in control group. Demographics, clinical history was recorded and biochemical analysis including Fasting Blood sugar, Total Cholesterol, Triglycerides and serum TSH and FT4 was done for each individual. The primary outcome was to find the correlation as assessed by the prevalence of subclinical hypothyroidism in patients having metabolic syndrome.

Results: The Mean±SD of age in this study was 49.05±11.18 years with a higher number of male gender compared to female (61.33% Vs 38.64%). The results of the study showed significantly higher number of patients with SCH in the study group compared to the control group (18.34 % Vs 7.19 %, p=0.00).

Conclusion: It is concluded that subclinical hypothyroidism is significantly correlated with metabolic syndrome.

Keywords: Central obesity, cardiovascular risk, Dyslipidemia, Metabolic syndrome, Subclinical hypothyroidism.

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Introduction:

Metabolic syndrome (MetS) is a condition characterized by a set of risk factors for cardiovascular (CV) disease including central obesity, high blood pressure (BP), high triglyceride (TG), low high density lipoprotein (HDL) cholesterol and high fasting blood sugar (FBS) levels.^{1,2} MetS is a common disease in the general population. The global incidence of MetS has increase from 1.1% to 3.85% during last 3 decades. MetS is documented as increasing a 5 fold risk of type 2 diabetes mellitus (Type-2 DM) and 2 fold increased risk of CV disease.^{3,4} The trends show that the patients with MetS are at high risk of developing

diabetes and suffering from CV disease in the coming years. Importantly the mortality rate related to high BMI has been estimated to increase by 28.3%. It is also important concern that impairment of thyroid Functions is also commonly seen in MetS.^{1,2,4} Increased level of thyroid stimulating hormone (TSH) in serum while normal level of free thyroxine (FT4) concentration is named as subclinical hypothyroidism (SCH). The global incidence of SCH in adult population is reported to be as high as 10%.⁵ most organ functions are affected by thyroid hormone and this hormone has a wide range of effects. Hence

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thyroid plays an important role in regulating the metabolism and metabolism of glucose and lipids, control of BP and energy consumption are affected by thyroid hormone in different ways.⁶ This hormone may be associated with metabolic syndrome because it serves as a general regulator of the metabolic process. It's not totally clear why obese people with metabolic syndrome have higher levels of thyroid hormones, like TSH and T3, but it's thought that it could be connected to insulin resistance because of a problem with post-receptor signals to the body's target tissue. There is a possibility that a mechanism similar to the insulin resistance exists for thyroid receptor resistance as well. Metabolic Syndrome and thyroid disorders are therefore both associated with an increased risk of developing atherosclerosis and CV diseases.⁷ Obesity causes thyroid hormone levels to rise and fall, while hypothyroidism leads to a slower metabolism that is a contributing factor to obesity. Therefore, it is unclear whether the rise or decrease in thyroid levels is due to MetS or a contributing cause.⁸

Correlation of SCH and CVD remains under discussion due to above mentioned risks. The studies working on this topic has however produced controversial results.^{9,10,11,12} The majority of the studies mentioned that the subclinical hypothyroidism increases the risk of MetS and its associated CV risk.^{9,10,11} Kannan et al in their study on thyroid dysfunction and CV outcomes provided evidence on increased CV risk in cases of SCH.¹³ Moon S conducted a meta-analysis on the correlation of SCH with CV risk and all-cause mortality and the results reported a positive correlation.¹⁴ There are, however, other studies that produce a negative correlation between SCH and MetS.^{12,15}

These observational studies indicate that SCH may be a biomarker for CV disease and is metabolic risk factors. This study was therefore planned to determine the correlation between MetS and SCH in patients reporting at the medical department of our hospital and diagnosed with MetS. The results of the study will be helpful in providing clear treatment guidelines for these patients to save them from the future complication especially the CV risks.

Material and Method:

Place of the study:

This case control study was conducted at the Department of Medicine, PAF Hospital Islamabad, Pakistan from 1st of March 2023 to 31st of August 2023.

Patient Population and Methodology of the Study:

Sample size was calculated using WHO sample size software.

Assumptions:

Alpha =5% (two sided), Power =90%

of laboratory investigations of patients regarding components of MetS are shown in Table-I.

p1= 14.6%, p2=7.2%

Estimated sample size: n1=278, n2=278.¹⁶

Sample Size:

A total number of 278 patients aging above 18 years, reporting at out-patient medical department of the hospital and diagnosed with metabolic syndrome were selected and enrolled in study group while another 278 individuals above 18 years old who were apparently looking healthier and were with no central obesity, hypertension or dyslipidemia were enrolled in control group.

Inclusion and Exclusion Criteria:

Exclusion criteria were set as individuals less than 20 years of age, pregnancy or lactation or already diagnosed cases of hypo or hyperthyroidism.

Demographics and clinical history was recorded for each individual including age, sex, body mass index (BMI) and visceral obesity. Clear history of any previous illness was recorded. Blood pressure was recorded for each individual as per standard protocol. Fasting blood samples were taken for fasting blood sugar, total cholesterol, triglycerides, high density lipoprotein cholesterol. Thyroid functions like TSH and FT4 were investigated. Metabolic syndrome was defined as per IDF which defines it as individuals with waist circumference (WC) > 94 cm in men or waist circumference (WC) > 80 cm in women plus presence of at least any two of the following. 1. Fasting blood glucose (FBG) >100 mg/dl or taking medication of DM. 2. High-density lipoprotein cholesterol (HDL-Cholesterol) < 40 mg/dl in men, < 50 mg/dl in women or taking medications for this indication. 3. Triglycerides (TG) >150 mg/dl or taking its medications. 4. Blood pressure > 130/85 mmHg or taking antihypertensive medication.² SCH was defined as TSH between 4.4 and 10 µm/L, with normal FT4 levels.¹⁷

The primary outcome was to find the correlation as assessed by the prevalence of subclinical hypothyroidism in patients having metabolic syndrome and significance of difference in the levels of TSH while levels of FT4 are comparable. A written consent was taken from the patients for the participation in study. Permission for conducting study was taken from the ethical committee of the PAF Hospital.

Data analysis: was performed using SPSS version 25. Mean± Standard deviation of quantitative variables was calculated. Qualitative variables were presented in shape of frequency and percentage. The variables were compared by applying Chi-square test and independent t-test while p≤0.05 was considered significant.

Results:

The Mean±SD of age in this study was 49.05±11.18 years with an age range of 29-73 years in overall study population. The number male gender was higher (61.33%) compared to female gender (38.66%). The group wise demographics, clinical findings and results

Table-I: The demographics, clinical findings and biochemical characteristics for both the groups. n=556				
Demographics, clinical findings and biochemical characteristics		Study group (n=278)	Control group (n=278)	p-value
Age (Mean±SD) years		49.85±11.91	48.25±10.37	0.09
Gender	Male n (%)	176 (63.3)	165 (59.35)	0.33
	Female n (%)	102 (36.69)	113 (40.64)	
BMI (Mean±SD)		31±3.48	29.19±4.28	0.00
Waist circumference (Mean±SD) cm		98.52±4.01	93.37±7.21	0.00
Systolic BP (Mean±SD) mmHg		142.68±8.55	127.4±14.89	0.00
Diastolic BP (Mean±SD) mmHg		90.73± 4.59	87.16±4.71	0.00
Fasting BG (Mean±SD) mg/dl		117.39±18.94	99.24±17.48	0.00
Triglycerides (Mean±SD) mg/dl		166.42±12.22	132.47±18.2	0.00
HDL Cholesterol (Mean±SD) mg/dl		46.85 ±10.79	50.06±9.09	0.00

The results show that number of the patients having SCH was significantly higher in the study group compared to the control group as shown in Table-II.

Table-II: Comparison of patients having SCH among the two groups n=556			
Presence of SCH	Study group (n=278)	Control group (n=278)	p-value
Yes n (%)	51 (18.34)	20 (7.19)	0.00
No n (%)	227 (81.65)	258 (92.8)	
Total	278	278	

The comparison of thyroid function between the 2 groups shows a significant correlation between MetS and SCH as the levels of SCH were significantly high in patients suffering from MetS compared to patients without MetS as shown in Table-III.

Table-III: Comparison of SCH levels between the two groups. n=556			
Thyroid Functions	Study group (n=278)	Control group (n=278)	p-value
FT4(Mean±SD) pmol/L	12.28±2.48	13.73±3.52	0.13
TSH(Mean±SD) (mIU/l)	3.63±1.96	2.71±1.65	0.00

Discussion:

Correlation between MetS and SCH has been discussed in a number of studies during last few years and the available data has provided some useful evidences over the topic.

Khatawada S conducted a cross-sectional study to find the correlation between MetS and thyroid functions. The results of the study proved a correlation between these two in 31.9% of the patients where most prominent was SCH which was observed in 26.6% of the patients. The study thereby concluded that thyroid dysfunction especially the SCH is commonly related to MetS where most common contributing factors were central obesity and HDL cholesterol.¹⁸ Bermúdez V et al published their research work on SCH and MetS in view of being important CV risk factors. The correlation between these two was proven in a way that out of patients diagnosed with SCH, 56.1% were also having MetS (p=0.03). Hyperglycemia was mentioned as the factor present in most of these MetS patients.¹⁹

Bhaskar MS studied the patients with MetS to find any prevalence of thyroid dysfunctions. The study results showed that out of 122 study patients having MetS, 57 (46.7%) of the patients had raised levels of TSH (TSH value>5) and 43(35.2%) were having SCH. Researchers therefore concluded that SCH is frequently found in

patients with MetS and evaluation of thyroid functions is recommended while treating these patients to reduce the future risk.²⁰

Prevalence of SCH in MetS was studied in Indian population by Badri PR. This cross-sectional study included the patients who were reporting at the OPD of General Medicine Department and were having MetS. Among the study population, 62.1% were having increased TG levels, 23.3% were having high total cholesterol levels while 30.1% were having raised levels of LDL cholesterol. The study reported an incidence of SCH as high as 30.1% of the patients who were having MetS. Among patients diagnosed with SCH 35.5% were also overweight compared to 18.1% in the control group.²¹

Hassanin HM planned a study to determine the association of SCH with MetS in young Egyptian patients. Out of the total study population, MetS was diagnosed in 23.9 % of the subjects and out of these subjects with MetS, the incidence of SCH was double than the subjects without MetS (14.6% Vs 7.2%). Hence a strong correlation between MetS and SCH was reported in this study (p<0.05). The predictors of SCH present in patients with MetS were reported as weight, body mass index and diastolic BP.¹⁶

A study recently published in 2023 by Abha P and co-workers focused on association of thyroid functions with MetS in view of lipid profiles of these patients. The results revealed that in patients with MetS, thyroid functions like TSH and T3 were also raised in addition to the components of MetS like WC, FBG, and TGs (p<0.001) as compared to subjects without MetS. The levels of TSH were significantly high in patients with metabolic syndrome compared to those without MetS (5.3±3.4 Vs 2.6±1.4 µl/mL, p<0.001).⁸

The Mean±SD of age in our study was 49.05±11.18 years with a higher number of males gender compared to females (61.33% Vs 38.64%). Parameters of MetS including waist circumference (98.52±4.01 Vs 93.37±7.21 cm, P=0.00), SBP (142.68±8.55 Vs 127.4±14.89 mmHg, P=0.00), DBP (90.73± 4.59 Vs 87.16±4.71 mmHg, P=0.00), FBG (117.39±18.94 Vs 99.24±17.48 mg/dl, P=0.00) and TG (166.42±12.22 Vs 132.47±18.2 mg/dl, P=0.00) and HDL cholesterol (46.85 ±10.79 Vs 50.06±9.09, P=0.00) were significantly higher in patients included in study group with MetS compared to subjects in control group.

The results of our study shows that prevalence of SCH was significantly high in study group as the number of the patients having SCH was significantly higher in the study group compared to the control group (18.34 % Vs 7.19 %, $p=0.00$). This prevalence is similar to reported in studies conducted previously over this topic and discussed above.^{16,18,19,20,21}

Similarly, the comparison of thyroid function between the 2 groups shows a significant correlation between MetS and SCH as the levels of SCH were significantly high (3.63 ± 1.96 Vs 2.71 ± 1.65 mIU/l, $p=0.00$) while there was no significant difference in levels of T4 among the two groups (12.28 ± 2.48 Vs 13.73 ± 3.52 pmol/L, $p=0.13$) in patients suffering from MetS compared to patients without MetS. These results are also similar to other studies which have worked on TSH in patients with MetS.^{8,20}

Hence, the patients with metabolic syndrome have been found to have a significantly higher incidence of SCH than the general population and while treating patients with MetS, thyroid dysfunction should also be taken into account to minimize the impending risk.

The major limitation of this study is that it was a single center study with limited sample size and only studied the correlation and not the outcomes. Future studies over this topic may be therefore helpful in adding more extensive data over the topic for preparing treatment guidelines for these patients.

Conclusion:

It is concluded that subclinical hypothyroidism is significantly correlated with metabolic syndrome. As MetS is known to be associated with mortality and morbidity, this correlation increase the focus on the potential benefits of treatment of subclinical hypothyroidism in terms of prevention of future adverse events.

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No

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