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ORIGINAL RESEARCH

Exploring the Association Between Components of Metabolic Syndrome and Thyroid Dysfunction: A Case-Control Approach

[1]Dr. Pankaj Kumar, [2]Dr. Sushil Kumar Kharwar, [3]Dr. Sudhir Kumar

[1]Associate Professor, [2,3]Assistant Professor, Department of General Medicine, T S Misra Medical College & Hospital, Lucknow, Uttar Pradesh, India

Corresponding author
Dr. Pankaj Kumar
Associate Professor, Department of General Medicine, T S Misra Medical College & Hospital, Lucknow, Uttar Pradesh, India

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ABSTRACT

Background: Thyroid dysfunction (TD) and metabolic syndrome are separate risk factors for atherosclerotic cardiovascular disease (CVD); their co-occurrence may significantly raise a person's chance of experiencing a cardiovascular event. Therefore, the purpose of our research was to assess the thyroid profile in individuals with MetS and investigate the connection between metabolic syndrome components and thyroid function tests. **Methods:** In this case control cross-sectional research, 120 patients with metabolic syndrome who were 20 years of age or older and satisfied the IDF (The International Diabetes Federation) panel's recommended criteria were included, along with 100 controls who were matched for age and sex. A recommended proforma was used to record the patient's anthropometric measurements, including height, weight, BMI, waist circumference, blood pressure, and a thorough medical history. Triglycerides, high density lipoprotein (HDL) cholesterol, free triiodothyronine (T3), free thyroxine (T4), and thyroid stimulating hormone (TSH) were measured in 5 ml of fasting venous blood samples. **Results:** The average age of the controls was 44.43±13.06 years (range 21-65 years), whereas the average age of the patients in the case group was 47.57±11.72 years (range 20-65 years). Age-wise, there was no statistically significant difference between the two groups (p=0.053). **Conclusion:** Thyroid dysfunction, especially overt and subclinical hypothyroidism, is common in people with metabolic syndrome, and women are more likely to have it. Their risk of CVD may rise as a result. Thyroid dysfunction screening is essential for improved treatment and early intervention. The cause-and-effect link should be investigated in future prospective research.

Key-words: Metabolic syndrome, thyroid dysfunction, cardiovascular disease, IDF panel, hypothyroidism.

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INTRODUCTION

The metabolic syndrome (MetS) is characterised by a number of risk factors that increase the risk of atherosclerotic cardiovascular disease and type 2 diabetes, including atherogenic dyslipidaemia, hypertension, glucose intolerance, and central obesity. These conditions are prothrombotic and pro-inflammatory [1, 2].

Because different regions have different sets of epidemic risk factors, the prevalence of MetS is rising globally. In India, it has also experienced a notable rise in prevalence, which has been attributed to mechanisation, increased migration to urban areas, and socioeconomic shifts towards greater affluence [3-5].

One of the most common endocrine conditions in the world is thyroid illness. An estimated 42 million Indians are thought to be affected by thyroid disorders, according to estimates from many research [5]. Given the significant regulatory role thyroid hormones play in blood pressure, cardiovascular function, lipid metabolism, and glucose metabolism, any dysregulation in thyroid function may be linked to MetS because the two conditions share characteristics like elevated triglycerides, insulin resistance, obesity, and reduced HDL-C, hyperglycemia, and hypertension [6, 7].

Since thyroid dysfunction (TD) and metabolic syndrome are both separate risk factors for the onset of atherosclerotic cardiovascular disease (CVD), having both conditions at the same time may make a person much more susceptible to cardiovascular

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events [8].

Numerous previous investigations on thyroid diseases in metabolic syndrome have produced conflicting and inconsistent findings regarding their incidence and relationship to metabolic syndrome components [9, 10]. If both conditions are present at the same time, thyroid function testing may be necessary to evaluate the elevated compounded risk of cardiovascular disease in metabolic syndrome. In order to better plan and manage the treatment of MetS patients and reduce their morbidity and mortality from cardiovascular events, our study set out to assess the thyroid profile in patients with the condition and investigate the relationship between thyroid function tests and metabolic syndrome components.

MATERIALS AND METHODS

Study Population

The study's convenience led to the selection of the sample size. After gaining their informed agreement, the research included all 120 patients with metabolic syndrome who were 20 years of age or older and satisfied the IDF panel's suggested criteria. These patients were either inpatients in the general medicine department or outpatients. The same hospital also provided 120 controls who were matched by age and sex. The research excluded pregnant women, patients using OC pills or other drugs that affect thyroid function and lipid levels, individuals with cardiovascular illness, any liver disease, and renal failure.

IDF criteria include central obesity (defined as waist circumference $\geq$90 cm for men and $\geq$80 cm for women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised TG levels: >150 mg/dL or specific treatment for this lipid abnormality.
- reduced HDL cholesterol: <40 mg/dL in males and <50 mg/dL in females, or specific treatment for this lipid abnormality
- raised blood pressure: Systolic BP >130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension.
- raised fasting plasma glucose (FPG) >100 mg/dL, or previously diagnosed type 2 diabetes.

Examination

Patient' s anthropometric measures like weight, height, BMI, and waist circumference and blood pressure along with detailed medical history were recorded in a prescribed proforma.

Biochemical investigations

Triglycerides, high density lipoprotein (HDL) cholesterol, free triiodothyronine (T3), free thyroxine (T4), and thyroid stimulating hormone (TSH) were measured in 5 ml of fasting venous blood samples. The EM-360 analyser was used to test the levels of blood glucose, triglycerides, and total cholesterol using an enzymatic approach. HDL cholesterol using a direct, homogenous technique. CLIA on ADVIA Centaur was used to assess serum free T3 (1.4– 4.2 pg/dL), free T4 (0.8– 2.0 ng/dL), and TSH (0.28– 6.82 IU/dL). If all thyroid hormone levels were within the standard range, the patient was considered euthyroid. Low levels of free T3 and free T4 and elevated TSH were considered indicators of overt hypothyroidism. If TSH was elevated while free T3 and free T4 were within the reference range, subclinical hypothyroidism was taken into consideration. When TSH was found to be normal or low with low fT4 levels, secondary hypothyroidism was taken into consideration. Subclinical hyperthyroidism was classified as TSH low with free T3 and free T4 within the reference range.

Statistical Analysis

Software called SPSS version 21.0 was used to do the statistical analysis. The program Microsoft Excel 2007 was used to create the tables and graphs. Numbers and percentages were used to display categorical variables. Mean ± standard deviation and percentages were used to represent all descriptive data. For continuous variables, the independent sample t test and one-way ANOVA were used, and for categorical variables, the chi square test was used with a 95% confidence interval. To determine the relationship between several continuous variables, Pearson's correlation analysis was used. Statistical significance was defined as $p<0.05$ for all statistical analyses.

RESULTS

The lowest number of instances in both categories were older than 60, while the highest number were between 51 and 60. The average age of the controls was 44.43±13.06 years (range 21-65 years), whereas the average age of the patients in the case group was 47.57±11.72 years (range 20-65 years). Age-wise, there was no statistically significant difference between the two groups (p=0.053).

The majority of individuals were female, regardless of the group. There was no statistically significant difference between the two groups (p=0.565).

Table 1: Comparison of two study groups for hemodynamic parameters

SN	Parameter	Cases		Control		Statistical significance	
		Mean	SD	Mean	SD	' t'	' p'
1.	SBP (mm of Hg)	138.67	15.10	125.61	8.78	9.063	<0.001
2.	DBP (mm of Hg)	85.93	7.88	80.24	5.96	7.697	<0.001

Both systolic as well as diastolic blood pressure levels of the cases were found to be significantly higher as

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compared to that in control group (p<0.001).

Table 2: Comparison of two study groups for Anthopometric and Biochemical Parameters

SN	Parameter	Cases		Control		Statistical significance	
		Mean	SD	Mean	SD	' t'	' p'
1.	Abdominal circumference (cm)	102.10	8.13	89.11	11.54	8.318	<0.001
2.	Fasting glucose (mg/dl)	167.11	55.43	95.23	15.77	13.738	<0.001
3.	Total cholesterol (mg/dl)	224.72	41.63	205.19	38.03	4.551	<0.001
4.	Triglyceride (mg/dl)	205.85	69.92	131.66	39.33	10.406	<0.001
5.	HDL (mg/dl)	44.92	11.27	53.97	6.68	-8.705	<0.001
6.	LDL (mg/dl)	139.81	39.26	126.08	34.26	3.707	0.008

Mean abdominal circumference, fasting glucose, total cholesterol, triglyceride and LDL levels of cases were significantly higher as compared to controls whereas mean HDL levels of cases were significantly lower as compared to that of controls.

Table 3: Comparison of two study groups for factors of metabolic syndrome

SN	Parameter	Cases		Control		Statistical Significance	
		No.	%	No.	%	χ^2	'p'
1.	Abdominal obesity	120	100	53	44.1	65.91	<0.001
2.	Hypertension	77	64.1	20	16.6	66.31	<0.001
3.	Raised Glucose	93	77.5	30	25	83.34	<0.001
4.	Raised Triglyceride	81	67.5	27	22.5	59.40	<0.001
5.	Low HDL	67	55.8	13	10.8	62.88	<0.001

A statistically significant difference (p<0.001) was seen between the two groups, with 100% of patients exhibiting abdominal obesity compared to 55.8% of controls.

The percentage of cases was substantially greater than that of controls for all major metabolic syndrome variables (p<0.001).

In contrast to controls, who had 19 (16.1%) positive results for none of the metabolic factors, 35 (32.2%) positive results for one factor, and 52 (49.3%) positive results for two metabolic syndrome factors, the majority of cases (n=40; 37.4%) had positive results for all five metabolic syndrome factors, followed by 36 (33.1%) positive results for four factors, and a total of 30 (25%) positive results for three factors.

Table 4: Comparison of Thyroid functions between two study groups

SN	Parameter	Cases		Control		Statistical significance	
		Mean	SD	Mean	SD	' t'	' p'
1.	TSH	5.23	3.46	4.34	3.35	3.601	0.011
2.	fT3	3.75	0.98	4.02	0.82	2.994	0.048
3.	fT4	0.98	0.38	2.37	0.39	8.640	<0.001

Cases had considerably higher mean TSH levels than controls (p<0.001), whereas cases had significantly lower mean T3 and T4 levels (including fT3 and fT4) than controls.

Thyroid problems were present in 33.2% of the patients. There were 31 (28.1%) instances of subclinical hypothyroidism, 3 (1,3%) of secondary hypothyroidism, and 4 (2,5%), of subclinical hyperthyroidism. Only seven people (8.7%) in the control group had a thyroid condition, and all of them had subclinical hypothyroidism. The two groups' differences were statistically significant (p<0.001).

Table 5: Association between Thyroid disorders and Different factors of metabolic syndrome

a) Cases

SN	Factor	Positive			Negative			Statistical significance
		Total	With thyroid disorder	% with thyroid disorder	Total	With thyroid disorder	% with thyroid disorder	
1.	Abdominal obesity	120	34	33.1	-	-	-	-
2.	Hypertension	77	24	30.2	27	12	41.1	χ^2=0.981; p=0.323
3.	Raised glucose	93	31	32.7	11	5	34.2	χ^2=0.009;

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								p=0.929
4.	Raised Triglyceride	80	29	35.1	23	7	24.7	χ^2=0.821; p=0.366
5.	Low HDL	67	21	30.4	37	15	38.4	χ^2=0.655; p=0.420

b) Controls

SN	Factor	Positive			Negative			Statistical significance
		Total	With thyroid disorder	% with thyroid disorder	Total	With thyroid disorder	% with thyroid disorder	
1.	Abdominal obesity	53	9	14.6	51	0	0	χ^2=8.231; p=0.008
2.	Hypertension	20	2	6.5	84	8	8.2	χ^2=0.071; p=0.792
3.	Raised glucose	30	2	4.5	74	8	9.2	χ^2=0.703; p=0.403
4.	Raised Triglyceride	27	5	13.1	77	6	5.3	χ^2=2.281; p=0.259
5.	Low HDL	13	4	19.1	91	7	6.5	χ^2=3.375; p=0.124

Every patient in the case group had abdominal obesity. Thyroid disorders were seen in 33.2% of the case group. Thyroid disorders were thus 33.2% common in obese people.

There were 53 instances of abdominal obesity in the control group, and 9 (14.6%) of those cases had subclinical hypothyroidism, a thyroid condition, compared to none without abdominal obesity. Consequently, a statistically significant correlation (p=0.008) is shown.

There was no statistically significant correlation found between the frequency of thyroid disorders and other variables in either the case or control groups (p>0.05).

Table 6: Association between Thyroid disorders and Age

SN	Factor	With thyroid disorder			Without thyroid disorder			Statistical significance
		n	Mean	SD	n	Mean	SD	
1.	Cases	34	50.21	9.85	70	47.46	8.78	t=1.351; p=0.181
2.	Controls	9	35.70	12.62	95	43.17	13.95	t=1.481; p=0.143

No significant association was observed between age and thyroid disorders in both the groups.

Table 7: Association between Thyroid disorders and Gender

SN	Factor	Male			Female			Statistical significance
		Total	With thyroid disorder	% with thyroid disorder	Total	With thyroid disorder	% with thyroid disorder	
1.	Cases	40	9	19.3	64	27	41.2	χ^2=6.193; p=0.024
2.	Controls	44	0	0	60	9	13.2	χ^2=6.450; p=0.021

For cases and controls independently, prevalence of thyroid disorders was higher in females as compared to males and this association was significant statistically too (p<0.05).

Table 8: Binary Logistic Regression to see the association of thyroid dysfunction with different metabolic syndrome factors and gender

	B	S.E.	Wald	df	Sig.	OR	95.0% C.I. for EXP(B)	
Male Gender	-2.383	.473	9.598	1	0.004	.252	.098	.633
Hypertension	-.418	.468	.798	1	0.372	.660	.265	1.646
Raised TG	.773	.502	3.374	1	0.124	3.165	.811	6.781
Low HDL	.130	.448	.084	1	0.774	1.139	.475	3.731

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Raised glucose	-.623	.685	.828	1	0.364	.538	.142	3.051
Metabolic syndrome	3.106	.824	7.559	1	0.011	9.221	1.640	42.222
Constant	-3.255	.465	24.598	1	<0.001	.106		

Thyroid dysfunction was shown to be always linked to abdominal obesity in the current investigation. For this reason, it was not included in the multivariate analysis. Based on the idea that thyroid dysfunction is influenced by independent factors such as gender, hypertension, elevated TG, elevated glucose, low HDL, and metabolic syndrome, a binary logistic model was therefore put out. Among the several independent factors examined, metabolic syndrome (p=0.011; OR=9.221; 95% CI=1.630-42.220) showed a significant positive correlation with the outcome, or thyroid dysfunction, whereas male gender had a significant negative association (p=0.004; OR=0.252; 95% CI=0.098-0.633).

DISCUSSION

Obesity, high blood pressure, dyslipidaemia (characterised by higher triglycerides and low levels of high-density lipoproteins), and hyperglycemia are all components of metabolic syndrome [11]. A total of 120 patients with metabolic syndrome were included in our research; their ages varied from 20 to 65, with a mean age of 46.58±10.73. Similar to earlier research, our study also found that the proportion of patients with metabolic syndrome increased with age, with the exception of those over 60. This could be explained by the strict exclusion criteria we employed, which made it challenging to identify metabolic syndrome patients in this age group who did not also have liver, renal, or congestive heart failure disorders [12, 13].

The male to female ratio was 0.61:1, with the majority of our cases (62%) being female. These findings align with the well-established findings from earlier research [14,15] indicating women are more likely than men to acquire metabolic syndrome.

The majority of participants (51%) in the control group also had metabolic syndrome characteristics, such as abdominal obesity. In contrast to 75%, 91%, 79%, and 65% of cases, a sizable portion of control subjects also had other metabolic syndrome factors, such as hypertension (18%), elevated glucose (28%), elevated triglycerides (25%), and low HDL (11%). These findings may be explained by the sedentary lifestyle of the current population, which influences the health status of the community.

The IDF criteria, which identify central obesity as a crucial component of metabolic syndrome, were used in the current investigation to evaluate metabolic syndrome. Since the IDF criteria take ethnic variance into account and ATP III is mostly suited to the American population, we decided to utilise it instead of NCEP: ATP III (National Cholesterol Education Program Adult Treatment Panel III).

Any imbalance in thyroid function may be linked to metabolic syndrome since thyroid hormones regulate blood pressure, cardiovascular function, and the metabolism of fats and carbohydrates [6, 7].

In this investigation, patients with metabolic syndrome had considerably higher mean TSH levels than the control group (p<0.05), and their mean fT3 and fT4 levels were significantly lower than those of the control group (p<0.05). Similar findings were also seen in other Indian investigations [16– 18]. In the populations with metabolic syndrome and those without, the prevalence of thyroid diseases (TD) was 32% and 7%, respectively, with a statistically significant difference (p<0.05). Two individuals had subclinical hyperthyroidism, one patient had secondary hypothyroidism, and the most prevalent thyroid condition among the cases was subclinical hypothyroidism (29 patients). All seven of the controls exhibited subclinical hypothyroidism. These findings were consistent with those of other earlier research [14, 19– 21].

Because various studies utilised different criteria for classifying thyroid disorders and metabolic syndrome, the prevalence of thyroid disorders in patients with metabolic syndrome varied from 26% to 78% in different series.

Abdominal obesity was revealed to be a powerful predictor of thyroid dysfunction in the current investigation since it was present in all controls with thyroid dysfunction. Thyroid dysfunction and obesity are recognised to be related, however it is still unclear whether this is a cause-or-effect relationship. Up to 44% of individuals with thyroid disorders were found to be obese in a research that assessed the relationship between thyroid disorders and obesity using a BMI criteria for obesity. On the other hand, 44% of the 450 patients who attended an obesity clinic had a thyroid condition [22].

None of the parameters in the preliminary study were substantially linked to thyroid dysfunction when the data was evaluated for associations between independent metabolic syndrome factors and thyroid dysfunction in individuals with MeS. The similar findings were seen in a few additional research [21, 23, 24]. Our findings, however, ran counter to those of a few other investigations that found a strong correlation [6, 16, 25]. Age, gender, genetics, nutrition, environment, and geographic location may all affect the patterns of thyroid abnormalities in MetS and how they are linked to other MetS components [1, 26, 27].

The current investigation did not find a significant correlation between age and thyroid disorders in either the patients or the controls. However, TD was more common in women with MetS than in males in our research (40.3% vs. 18.4%). This was consistent with findings reported in previous investigations [6, 21, 28].

In line with the results of the univariate evaluation,

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the current study's multivariate logistic regression showed that the outcome, a thyroid disease, was substantially correlated with both female gender and the existence of metabolic syndrome. These results appear reasonable and rationalistic, considering that thyroid dysfunction and metabolic syndrome are more prevalent in women in this region of the globe. Because thyroid dysfunction is strongly linked to metabolic syndrome, a major lifestyle condition, the results also highlight the rise of thyroid dysfunction as an impending serious lifestyle danger. For improved therapeutic care, it also justifies the development of a systematic method for assessing if thyroid dysfunction is present in individuals with MetS.

CONCLUSION

Thyroid dysfunction, including subclinical and overt hypothyroidism, was shown to be more prevalent in patients with metabolic syndrome, with females being more at risk. Patients with metabolic syndrome who also have hypothyroidism may be at increased risk for cardiovascular disease (CVD) since both conditions are independent risk factors for obesity and atherosclerotic illnesses. As a result, it requires that these patients be screened for thyroid dysfunction, which might help with early intervention and improved patient management to lower the risk of a negative cardiovascular event and improve prognosis. Future prospective studies with large sample sizes are necessary to investigate the causal link between thyroid problems and metabolic syndrome.

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