Hypothyroidism and its influence in the development of metabolic syndrome- A cross sectional study

Dr. Kiran Tandia[1], Dr. Leena Parihar[2], Dr. Vishnu Gupta[3], Dr. Poonam Mishra[4]

[1]Associate Professor, Department of Medicine, Birsa Munda Government Medical College, Shahdol, Madhya Pradesh, India
[2]Assistant Professor, Department of Community Medicine, N.S.C. Government Medical College, Khandwa, Madhya Pradesh, India
[3]Demontrator, Department of Community Medicine, SRVS Medical College, Shivpuri, Madhya Pradesh, India
[4]Demonstrator, Department of Pathology, NSCB Medical College, Jabalpur, Madhya Pradesh, India**(Corresponding author)**

Abstract:

Background: Patients with hypothyroidism including subclinical hypothyroidism have a higher chance of developing the metabolic syndrome. In the current cross-sectional investigation, the relationship between metabolic syndrome and hypothyroidism was examined. **Methodology:** A cross sectional study was carried out in the General Medicine department of a tertiary care hospital. Patients were classified based on the thyroidism status. Various parameters of metabolic syndrome were correlated with TSH Levels. **Results:** It has been observed that the prevalence of hypothyroidism in Metabolic Syndrome is found to be 41.36%. Significant direct relationship was observed between TSH levels and HbA1c, Fasting Blood Sugar, Triglycerides and Body Mass Index and a significant inverse relationship was observed with HDL cholesterol. **Conclusion:** Hypothyroidism is found to be one of the serious risk factors for development of metabolic syndrome. It is further associated with multiple components of Metabolic syndrome. Hence a regular screening of thyroid levels can be useful in prognosis of Metabolic Syndrome.

Keywords: Hypothyroidism, Metabolic Syndrome, Thyroid Stimulating Hormone.

Introduction:

A group of risk factors known as the metabolic syndrome includes hypertension, atherogenic hyperlipidemia, diabetes, endothelial dysfunction, and inflammatory diseases. Increased risk for type 2 diabetes mellitus and atherosclerotic heart diseases is linked to this group of metabolic disorders.[1] currently, it appears that there are several underlying risk factors for metabolic syndrome, the most significant of which are central obesity and insulin resistance. Physical inactivity, ageing, hormone imbalance, and genetic or ethnic predisposition are other conditions that are related.

The metabolism of glucose and lipids, the control of blood pressure, and energy expenditure are all impacted in various ways by thyroid hormones.[2] Patients with hypothyroidism including subclinical hypothyroidism have a higher chance of developing the metabolic syndrome, according to recent studies.[3,4] According to research, those with thyroid stimulating hormone (TSH) levels above the normal range (2.5–4.5 mU/L) were more likely to be obese, have higher TG levels, and be at an increased risk of developing the metabolic syndrome.[5] Even though TSH levels are within the normal range, healthy young women with TSH levels > 2.5 mU/L must be examined for metabolic syndrome. Due to a variety of factors, including altered insulin secretion and lipid levels, thyroid diseases, including both hypo- and hyperthyroidism, have been linked to insulin resistance. Attenuated baseline plasma insulin is a feature of overt hypothyroidism (OH) and subclinical hypothyroidism (SH), and insulin sensitivity may increase with substitution therapy.[6]In the current cross-sectional investigation, the relationship between metabolic syndrome and hypothyroidism was examined.

Additionally, elevated prevalence of metabolic syndrome was substantially correlated with high normal TSH levels and low normal free T4 levels, which may be crucial when assessing such people.[7] because hypothyroidism increases the risk of developing metabolic syndrome, hypothyroidism

should be taken into account in individuals who have just been diagnosed with the condition. According to the aforementioned studies, hypothyroidism has a higher risk of developing the metabolic syndrome.[8] the link between hypothyroidism and atherosclerotic illnesses such ischemic heart disease, cerebrovascular disease, and peripheral vascular disease may be influenced by metabolic syndrome.

Methodology:

Study Design:

A cross sectional study was carried out in the General Medicine department of a tertiary care hospital for a period of 9 months from February 2022 to November 2022. The sample size was estimated to be 200 based on the prevalence in the hospital. A written informed consent was obtained from all the study participants. Based on the prevalence of metabolic syndrome in the study site, the sample size was estimated to be 218 patients at 95% confidence interval.

Patient Selection:

Adult Patients above 18 years diagnosed with clinical hypothyroidism with elevated TSH levels or clinically euthyroid patients are included in the study. Patients with nodules who were subjected for FNAC and diagnosis belonging to levels BETHESDA I to IV were included in our study. Patients who are younger than 18, pregnant and have nodules diagnosed with BETHESDA V and above were excluded from our study. Also, it was ensured that patients who have recently used Iodine contrast as diagnostic agent over last 3 months were excluded from the study. Patients who had thyroidectomy are also not included in our study. Metabolic syndrome was determined only by ATP III criteria. In our study, overt hypothyroidism is considered TSH > 5.0 mU/L and FT4 < 9.5 pmol/L.

Study Procedure:

A specially designed Performa was used to collect demographics such as age, sex, family history, co morbidities, social history and anthopometric measurements. Blood samples were collected after overnight fasting. The parameters such as TSH, Free T3, Free T4 , Fasting Blood Sugar, Glycated Hemoglobin , Lipid Profile were assessed. Six mL of fasting venous blood was collected from all the participants into anticoagulated tube (1mL) and plain tube (5mL). Samples were separated by centrifugation and stored at -50^{o} C until further biochemical analysis

Statistical Analysis:

The data of metabolic syndrome patients were categorized as 3 groups – Overt hypothyroidism, Subclinical and Euthyroid patients. ANOVA followed by Dunnett's test was performed to understand the significance of various metabolic markers. Correlation analysis was performed to identify the pattern of hypothyroidism and its impact on metabolic syndrome. All the tests are performed at significance level of 95% and a p value of less than 0.05 is considered significant.

Results:

We have initially screened 296 patients of metabolic syndrome based on the inclusion and exclusion criteria and following subject consent we have finally included 220 patients for this study. The details of the patient selection are provided in Fig 1. The baseline characteristics of the selected patients were provided in Table 1.

Figure 1: Patient Selection criteria

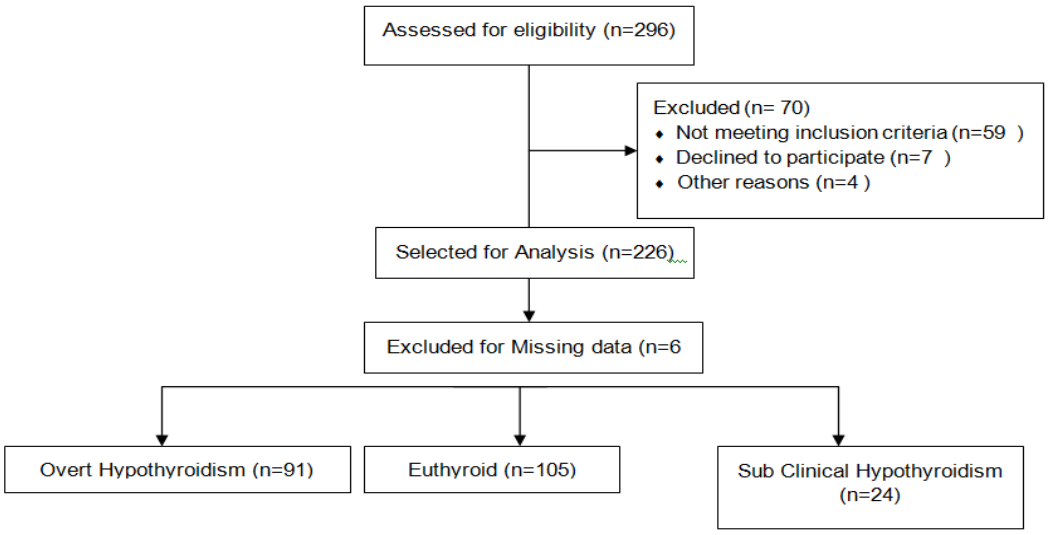

Table 1: Baseline Characteristics

Parameter	Hypothyroidism (n=91)	Euthyroid (n=105)	Sub-Clinical (n=24)
Age in Years (Mean±SD)	37.22±6.21	39.15±5.41	40.21±7.10
Male	19 (20.87)	37 (35.23)	7 (29.16)
Anthropometric Measurements			
Height in cm (Mean±SD)	157.23±7.11	161.22±6.10	159.32±5.99
Weight in Kg (Mean±SD)	79.25±2.14	70.94±2.95	69.10±3.11
BMI	29.12±1.62	25.14±2.01	24.12±2.31
Waist circumference in cm (Mean±SD)	102.25±5.71	91.21±3.74	87.26±6.11
Hip Circumference in cm (Mean±SD)	117.26±4.15	104.61±3.92	114.21±3.21
Smoking Status			
Smoker	21 (23.07)	29 (27.61)	7 (29.16)
Past Smoker	19 (20.87)	19 (18.09)	2 (8.33)
Non Smoker	51 (56.04)	57 (54.28)	15 (62.5)
Alcohol Status			
Alcoholic	31 (34.06)	34 (32.38)	07 (29.16)
Non Alcoholic	60 (65.93)	71 (67.62)	17 (70.83)

Comorbidities			
Diabetes Mellitus	88 (96.70)	91 (86.67)	23 (95.83)
Hypertension	73 (80.21)	84 (80.00)	21 (87.50)
Asthma	2 (02.19)	1 (0.95)	1 (04.16)
COPD	3 (03.21)	3 (2.85)	0 (0.00)
Cardiovascular Diseases	15 (16.48)	21 (20.00)	3 (12.5)
Osteoarthritis	11 (12.08)	7 (06.67)	2 (8.33)

All values are n (%) unless otherwise mentioned. P<0.05 is considered significant. It has been observed that the prevalence of hypothyroidism in Metabolic Syndrome is found to be 41.36%. The mean age is around 39 years of age.

Table 2: Components of Metabolic Syndrome

Parameter	**Hypothyroidism (n=91)**	**Euthyroid (n=105)**	**Sub-Clinical (n=24)**
Fasting Blood Glucose mg/dL	157.26±11.10*	147.23±7.12	141.37±5.32
HbA1c	8.94±0.59**	7.97±0.31	7.54±0.32
Systolic Blood Pressure mmHg	144.38±7.22*	139.41±6.10	137.25±5.11
Diastolic Blood Pressure mmHg	94.21±5.10*	91.20±4.32	87.22±3.71
HDL mg/dL	27.65±7.01**	34.21±6.32	35.11±5.94
Waist circumference in cm	102.25±5.71*	91.21±3.74	87.26±6.11
Triglycerides mg/dL	221.21±17.42**	191.51±14.15	182.55±19.21

All values are Mean±SD unless otherwise mentioned. *P<0.05 is considered significant, **p<0.0001 considered extremely significant. It is clearly evident from Table 2 that HbA1c had a very significant correlation with Hypothyroidism.

Table 3: Linear regression analysis of variables with TSH Levels

Parameter	***R***	r^2	***p* value**
Age	0.3162	0.0999	0.0517
BMI	0.7193	0.5173	0.0021*
Smoker	0.5771	0.3330	0.0315*
HbA1c	0.7721	0.5961	<0.0001**

FBS	0.7142	0.5100	0.0027*
HDL	-0.6971	0.4859	0.0037*
Triglycerides	0.6210	0.3856	0.0214*

*P<0.05 is considered significant, **p<0.0001 considered extremely significant. Significant direct relationship was observed between TSH levels and HbA1c, Fasting Blood Sugar, Triglycerides and Body Mass Index and a significant inverse relationship was observed with HDL cholesterol.

Discussion:

In controlling the metabolism of glucose, lipids, and energy balance, thyroid hormones (TH) are crucial. Studies have been done on certain elements of the metabolic syndrome in relation to thyroid health.[9] Serum TSH levels have been linked positively to BMI, arterial hypertension, particularly diastolic hypertension, serum cholesterol, and triglyceride levels in numerous investigations of the general population. We hypothesized that the combined burden of hypothyroidism and metabolic syndrome, if present concurrently, would offer a greater concern given that metabolic syndrome per se increases cardiovascular risk. We found that hypothyroid people had a two to three times greater risk of having the metabolic syndrome than euthyroid ones in this cross sectional research.[10]

In general, men were more likely than women to have the metabolic syndrome, and women with overt hypothyroidism were more likely to have it. Men's metabolism was more obviously impacted by overt hyperthyroidism than it was by women's metabolism.[11] Compared to men; women's metabolic state was more vulnerable to overt and subclinical hypothyroidism. Further research revealed that changes in lipid metabolism and elevated risks of abdominal obesity and hypertriglyceridemia were principally responsible for the influence of hypothyroidism on the incidence of metabolic syndrome in women.[12] Overall, women with hypothyroidism are more likely than males to develop metabolic syndrome. Additionally, our investigation discovered distinct thyroid dysfunction effects on the metabolic syndrome and its elements.[13]

The fact that most of these studies assessed the effects of TSH level on metabolic syndrome rather than thyroid dysfunction as a whole may account for differences in these results. In one part of the study, only metabolic syndrome elements related to serum TSH levels were examined; in the other, TSH, FT3, and FT4 were examined as factors. Age, sex, nationality, and many other characteristics may all have an impact on the intricate interaction between TSH, FT3, and FT4 and metabolic parameters. The conclusions cannot be applied to the broader population due of the wide variations in how these characteristics are distributed among various communities.

The limitations of the study include all participants had their serum TSH levels checked; only those individuals with abnormal thyroid function had their FT4 and FT3 levels checked. The levels of insulin and sex hormones were not assessed. As a result, it was not possible to study each of these affecting factors separately. The causative link between thyroid function and metabolic syndrome cannot be verified because this study was cross-sectional rather than cohort, and further prospective studies should be conducted to clarify causality.

Conclusion:

The relationship between thyroid malfunction and metabolic syndrome varied depending on the BMI. Particularly in obese patients, overt hypothyroidism was linked to an increased risk of metabolic syndrome. The alteration could be a result of TSH's impact on blood lipid levels. Large scale studies are required to assess the relevance of early diagnosis of thyroid dysfunction, particularly in the subclinical form, and the long-term connection with metabolic syndrome in diverse age, sex, and BMI groups.

Conflicts of interest:

None

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None

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