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A COMPARATIVE ANALYSIS OF SUBCLINICAL HYPOTHYROIDISM IN INDIVIDUALS WITH METABOLIC SYNDROME VERSUS THOSE WITHOUT METABOLIC SYNDROME: A CROSS-SECTIONAL STUDY.

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ABSTRACT.

Aim: The objective is to compare the thyroid status of people with metabolic syndrome (MetS) to that of healthy controls.

Methods: This cross-sectional study was conducted in the general medicine department of a tertiary care hospital in India for a duration from February 2021 to March 2022. The study had a total sample size of 50, which consisted of 25 matched cases with metabolic syndrome and 25 controls. Chemiluminescence2 hormone analyzer, the chemiluminescence test was used to analyze T3, T4, and TSH. Through internal and external quality initiatives, the biochemical assays were regularly observed.

Results: Of the study population, 55% of the controls were male and 45% were female, while there was a little female predominance of 57% female and 41% male among the cases. The study population's mean age was 47.36 ± 11.20 for controls and 50.21± 9.86 for cases. There was a significant difference (p-value < 0.0001) among the patients and controls in every Met S component. TSH revealed a significant difference, with the mean TSH in the control being 3.01± 0.32 while in the cases being 8.32 ± 3.02. The most common type of thyroid dysfunction in people with Met S is subclinical hypothyroidism (SCH), which is seen in 23% of cases. Overt hypothyroidism is found in 5% of cases, whereas there are no occurrences of overt hyperthyroidism.

Conclusion: A high frequency of TD was seen in individuals with metabolic syndrome, suggesting a potential interaction between metabolic syndrome and thyroid function. The most common TD among Indian MetS patients was hypothyroidism.

Recommendation: Since metabolic syndrome (MetS) patients have a high prevalence of thyroid dysfunction (TD), healthcare providers should consider routine thyroid function assessments, especially for subclinical hypothyroidism, the most common thyroid disorder in this population. Additional research is needed to understand how MetS affects thyroid function.

Keywords: *Thyroid stimulating hormone, Central obesity, Metabolic syndrome, Hypothyroidism*
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INTRODUCTION.

Metabolic syndrome (MetS) components have been related to elevated serum thyroid stimulating hormone levels. Research comparing euthyroid and subclinical hypothyroid persons has revealed that the former group has greater incidences of dyslipidemia and hypertension [1]. TSH levels are inversely correlated with HDL and positively correlated with BP, total cholesterol, triglycerides, and LDL even in the euthyroid range [2]. In people with subclinical hypothyroidism, population-based studies have found decreased HDL and greater triglycerides, as well as a strong association between blood TSH and obesity [3]. Furthermore, euthyroid persons' serum TSH has been linked in cross-sectional studies to increased triglycerides and a greater risk of MetS. Serum TSH was related to lower levels of HDL, TC, abdominal girth, and BP, and higher levels of triglycerides, TC, and blood pressure, according to a different study that included a 3-year follow-up period. Serum TSH levels increased over time in subjects with metabolic syndrome [4].

The majority of this research, however, was conducted on younger populations, and older people may have a different relationship between serum TSH and metabolic syndrome. Compared to those with subclinical hyperthyroidism, older Taiwanese people with subclinical hypothyroidism had a greater frequency of metabolic syndrome. In the same cohort, TSH was strongly correlated with BP, lipids, and a higher incidence of MetS [5]. More recently, Waring *et al*. found that there was a stronger correlation between the risk of prevalent MetS and higher blood TSH amount, even when TSH was in the normal range. There was a strong correlation found between a higher frequency of MetS and subclinical hypothyroidism with a TSH level below 10 mU/l [6].
It's critical to investigate the connection between metabolic syndrome and serum TSH, particularly in older people, given the rising number of elderly people. The study aimed to evaluate the thyroid status in persons with metabolic syndrome in comparison to healthy controls, and thyroid status was found to be associated with components of metabolic syndrome.

METHODS.

Study Design.

The present investigation was a cross-sectional study.

Study setting.

The study was carried out at the Department of General Medicine, Faculty of Medicine KBN University, Kalaburagi, Karnataka, India, spanning a period of February 2021 to March 2022.

Participants.

The study cohort comprised individuals who exhibited no signs of illness or abnormality and were therefore classified as control subjects. The study encompassed a comprehensive sample size of 50 participants, consisting of 25 individuals diagnosed with Metabolic Syndrome (MetS) and an equivalent number of 25 control subjects.

Inclusion Criteria.

Participants with diabetes-related complications.

Exclusion Criteria.

Individuals presenting with hepatic and renal impairment, who are concurrently administered corticosteroids or other pharmacological agents that modulate lipid, glucose, or thyroid levels, Pregnant individuals or participants with a medical background of cardiovascular disease.

Ethical considerations.

Written informed consent was taken from all the participants before the study.

Analysis Protocol.

Following the acquisition of informed consent, the study group underwent assessments of abdominal girth and BP. The participants were instructed to provide samples following an overnight period of fasting. In a sterile environment, a total of 5 milliliters of blood was collected using non-additive vacutainers. Subsequently, the collected blood samples were subjected to centrifugation and subsequently analyzed. The enzymatic assay on the Beckman Coulter AU480, a fully automated clinical chemistry analyzer, was utilized to evaluate the lipid profile and fasting blood glucose. Thyroid function tests, encompassing the measurement of T4, TSH, and T3 were subjected to meticulous analysis utilizing a chemiluminescence assay on the Access-2 hormone analyzer. Biochemical assays were consistently observed via internal and external quality programs.

Statistical Analysis.

Subjects who fulfilled the NCEP ATP III criteria, characterized by the presence of at least three out of the five following components, were classified as cases:

- In males, an abdominal girth is more than 40 inches while in females, an abdominal girth surpassing 35 inches is indicative of an increased abdominal girth.
- The presence of fasting blood glucose levels exceeding 100 mg/dl or the utilization of therapeutic interventions to manage such levels.
- Elevated triglyceride levels exceeding 150 mg/dl or under therapeutic intervention.
- The levels of HDL cholesterol, in males, are considered to be below the desirable threshold when they fall below 40 mg/dl. Similarly, in females, HDL cholesterol levels are deemed suboptimal when they are less than 50 mg/dl.
- The patient demonstrates increased systolic blood pressure levels surpassing 130 mmHg as well as diastolic blood pressure levels exceeding 85 mmHg or is presently undergoing therapeutic interventions for hypertension.

The variables about MetS were stated in the form of mean and SD.

RESULTS.

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The present study comprised a control group consisting of 55% males and 45% females. In contrast, the cases exhibited a slightly higher proportion of females at 57%, with males accounting for 41% of the sample. The average age between the cases was 50.21 ± 9.86 years, whereas between the control subjects, it was 47.36 ± 11.20 years.

Table 1: Comparing the MetS components between the cases and the controls.

Parameters	Cases (Mean ± SD)	Controls (Mean ± SD)	'p' value
Fasting blood glucose (mg/dl)	109 ± 80.31	44.5 ± 9.74	<0.0001
Abdominal girth (inches)	20.15 ± 2.35	16.4 ± 2.31	<0.0001
Triglycerides(mg/dl)	102.5 ± 72.6	56.4 ± 30.23	<0.0001
HDL (mg/dl)	16.5 ± 6.1	20.5 ± 5.1	<0.0001
Systolic blood pressure(mmHg)	70.5 ± 9.21	61.7 ± 8.22	<0.0001
Diastolic blood pressure(mmHg)	47.48 ± 4.7	40 ± 3.2	<0.0001
T3 (ng/ml)	0.76 ± 0.09	0.90 ± 0.14	0.1
T4 (µg/dL)	9.02 ± 1.7	8.4 ± 1.6	0.2
TSH (µIU/ml)	8.32 ± 3.02	3.01 ± 0.32	0.034

Table 1 displays the mean values associated with triglyceride levels, abdominal girth, fasting blood glucose, systolic and diastolic blood pressure, and high-density lipoprotein. These parameters are essential components of MetS and were observed in both the cases and controls. There was a significant difference (p-value < 0.0001) among the patients and controls in every Met S component.

The investigation additionally evaluated the thyroid panel, encompassing T3, T4, and TSH, within the cohort under examination. The TSH exhibited a statistically relevant disparity (p = 0.02) between the two groups, with an average TSH level of 8.32 ± 3.02 in the cases and 3.01 ± 0.32 in the controls. Nevertheless, a notable disparity in T3 and T4 concentrations was not observed among the two cohorts.

Subclinical hypothyroidism (SCH) emerged as the prevailing manifestation of thyroid dysfunction, with a prevalence of 23% among patients diagnosed with MetS, subsequently succeeded by overt hypothyroidism at a rate of 5%. No instances of manifest hyperthyroidism were observed.

There was a positive correlation observed between abdominal girth and high TSH levels, with statistical significance (p = 0.02). The HDL, blood pressure, and fasting blood glucose exhibited an inverse relationship with TSH. Conversely, triglyceride levels demonstrated a positive association with elevated TSH levels. However, it is important to note that none of these associations reached statistical significance.

DISCUSSION.

The present study revealed notable disparities in the baseline characteristics of individuals diagnosed with MetS when comparing the case group to the control group. These observations are consistent with the results reported in the studies conducted by Meher *et al*. [7] and Gywali *et al*. [8]. In these studies, it was observed that various biochemical and anthropometric measurements associated with components of MetS were significantly elevated in the cases group compared to the controls. However, it is worth noting that the levels of HDL, a type of lipoprotein, were found to be lower in the cases group. Obesity is known to exert a significant impact on glucose metabolism, primarily through the induction of insulin resistance, ultimately resulting in the development of hyperglycemia. Insulin resistance may exert an influence on hypertension, either through direct or indirect mechanisms, by impacting the process of renal sodium reabsorption. Elevated levels of triglycerides and reduced levels of HDL have been observed to contribute to an increase in LDL cholesterol, a known factor associated with atherogenesis. Hence, a robust association exists among the components of MetS.

The outcomes of the current study indicate a greater incidence of thyroid dysfunction (TD) among female individuals diagnosed with MetS compared to their male counterparts. The findings of this study are reliable with the findings reported in prior investigations carried out by Gywali *et al*. [8], Katiwada *et al*. [9], and Shantha *et al*. [10]. The findings of the thyroid function tests revealed a significant rise in TSH levels among individuals diagnosed with MetS. In contrast, no statistically relevant variation was noted in the levels of T4 and T3 among the two cohorts. The findings of this study align with the research conducted by Chugh *et al*., [11], wherein a statistically significant disparity was exclusively observed in the concentrations of TSH among the different cohorts. Gyawali *et al*. [8] observed noteworthy alterations in both TSH and free thyroxine (fT4) concentrations, demonstrating statistical significance. Elevated concentrations of TSH in conjunction with within-normal-range concentrations of T3 and T4 are indicative of an increased vulnerability to SCH that is associated with MetS. Elevated levels of TSH in individuals with obesity may potentially be associated with the hormone leptin, which is known to be heightened in cases of obesity. Leptin, in turn, can exert an influence on the hypothalamic-pituitary axis, thereby resulting in an upregulation of TSH synthesis [12].

In the present investigation, an examination was conducted wherein it was observed that thyroid dysfunction was detected in 31% of patients diagnosed with MetS. Among the identified cases, the prevailing pattern was that of SCH, accounting for 23% of the total, while overt hypothyroidism was observed in 5% of the affected individuals. No instances of hyperthyroidism were detected. Gyawali *et al*. [8] reported comparable prevalence rates of thyroid dysfunction, with SCH emerging as the prevailing pattern. SCH has the potential to induce hyperglycemia as a result of its influence on glucose transporters and gluconeogenesis. While overt hypothyroidism is recognized to be correlated with weight gain and obesity, emerging evidence indicates that SCH is also associated with substantial weight gain. Hence, a significant convergence can be observed in the pathophysiological mechanisms underlying MetS and SCH [13].

The relation between components of MetS and thyroid dysfunction has exhibited incongruity in prior investigations, potentially attributable to divergent factors such as ethnic disparities, lifestyle disparities, racial disparities, age disparities, and gender disparities within the cohorts under study [14, 15]. In the present investigation, the findings indicate a lack of statistically significant associations between the various constituents of MetS and thyroid hormones, except abdominal girth. Previous research has demonstrated significant correlations among thyroid function, lipid profiles, and insulin resistance, ultimately culminating in the development of hyperglycemia [14, 16].

CONCLUSION.

Thyroid dysfunction, particularly subclinical hypothyroidism, exhibited a higher prevalence among patients diagnosed with MetS. Therefore, it is crucial to conduct a thorough screening of patients diagnosed with MetS to identify any potential thyroid dysfunction, as this is essential in mitigating the risk of mortality associated with cardiovascular complications.

LIMITATIONS.

It is important to acknowledge that the study's relatively smaller sample size might have imposed certain limitations on the capacity to identify and establish these associations. Further investigation is warranted to establish definitive associations between thyroid dysfunction and components of MetS through the implementation of large-scale epidemiological studies. Moreover, the inherent cross-sectional design of this study precludes the establishment of causality, while the utilization of free T3 (fT3) and free T4 (fT4) measurements may yield a more precise assessment of thyroid function.

RECOMMENDATION.

Given the high prevalence of thyroid dysfunction (TD) among individuals with metabolic syndrome (MetS), healthcare providers should consider routine thyroid function assessments in MetS patients, especially for subclinical hypothyroidism, as it appears to be the most common thyroid disorder in this population. Further research is needed to explore the underlying mechanisms of the interaction between MetS and thyroid function.

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LIST OF ABBREVIATIONS.

MetS- Metabolic syndrome
SCH- Subclinical hypothyroidism
TSH- Thyroid-stimulating hormone
HDL- High-density lipoprotein
TC- Total cholesterol
BP- Blood pressure
TD- Thyroid dysfunction

CONFLICT OF INTEREST:

The author declares no conflict of interest.

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