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Observational investigation of the clinico-epidemiological features of thyroid dysfunction (TD) in people with metabolic syndrome (MetS)

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Abstract
Aim: The aim of the present study was to assess the prevalence and clinical and epidemiological factors of thyroid dysfunction (TD) in Indian patients diagnosed with metabolic syndrome (MetS).
Methods: The study was conducted within the Department of General Medicine for the period of 1 year. In this study, a total of 300 patients diagnosed with Metabolic Syndrome (MetS) were included for enrollment.
Results: In this study, a total of 300 patients diagnosed with Metabolic Syndrome (MetS) were included for enrollment. In both groups, there was a prevalence of female dominance over males. The mean height in the first group was 164.0±9.01, while in the second group it was 161.9±8.52. The mean weight in the groups was 79.4±13.13 and 75.8±12.29, respectively. Among the cohort of 300 patients diagnosed with Metabolic Syndrome (MetS), it was observed that 60 individuals (20%) presented with hypothyroidism, while 6 individuals (2%) exhibited overt hyperthyroidism.
Conclusion: The observed prevalence of thyroid dysfunction (TD) among patients diagnosed with metabolic syndrome (MetS) was found to be significantly elevated, suggesting a potential correlation between thyroid function and MetS. The data obtained from the current study will assist in establishing a correlation between thyroid dysfunction (TD) and metabolic syndrome (MetS). The early identification of TD in individuals with MetS would be beneficial for implementing timely interventions, such as lifestyle modifications, to potentially alter the progression of the disease.

Keywords: Metabolic syndrome, hypothyroidism, subclinical hypothyroidism, thyroid dysfunction

Introduction
Based on extant research, it has been determined that metabolic syndrome affects around 25-35% of the adult populace in India [1]. As to the recommendations established by the National Cholesterol Education Programme Adult Treatment Panel–III, the diagnosis of metabolic syndrome is confirmed when an individual presents with a minimum of three out of the five specified disorders [2]. The growth in mechanization, reduction in physical activity, and the intake of high-fat, quick, and unhealthy food have contributed to a higher occurrence of obesity and insulin resistance, leading to the development of metabolic syndrome. The prevalence rates of non-communicable diseases (NCDs) are significantly elevated in those diagnosed with metabolic syndrome [3, 4]. The timely identification of characteristics that can predict the development of metabolic syndromes, such as hypertension and obesity, along with the implementation of appropriate interventions, can contribute to the prevention of non-communicable diseases, including diabetes and cardiovascular disease.
Numerous recent investigations have shown evidence of a link between metabolic syndrome and thyroid dysfunction. Thyroid dysfunction refers to the presence of changes in the levels of thyroid-stimulating hormone, with or without concurrent alterations in Triiodothyronine (T3) and Tetraiodothyronine (T4). Individuals exhibiting elevated levels of Thyroid-stimulating hormone (TSH) were observed to possess a twofold increase in the occurrence of metabolic syndrome [5]. An association has been shown between subclinical hypothyroidism characterized by elevated levels of thyroid-stimulating hormone (TSH) and an increased risk of developing coronary heart disease. Both atherosclerosis and dyslipidemia are prevalent in individuals with hypothyroidism [6].

Thyroid problems rank among the most frequent endocrine disorders on a global scale. According to estimates derived from many research, it has been anticipated that over 42 million individuals in India are afflicted with thyroid disorders [7]. Metabolic syndrome (MetS) exhibits a strong correlation with thyroid dysfunction (TD) owing to the influence of thyroid hormones on lipid metabolism, glucose regulation, blood pressure, and cardiovascular impairment [8]. There may be a correlation between alterations in thyroid gland function and the presence of Metabolic Syndrome (MetS) and its associated factors, such as obesity, insulin resistance (IR), abnormalities in lipid and glucose metabolism, elevated blood pressure, and cardiovascular dysfunction. Metabolic syndrome (MetS) and type 2 diabetes (TD) share a set of similar disorders, including abdominal obesity, hyperglycemia, hypertension, lower levels of high-density lipoprotein cholesterol (HDL-C), and raised levels of triglycerides (TG). Furthermore, insulin resistance (IR), which is recognized as a fundamental mechanism underlying metabolic syndrome (MetS), also contributes to the development of hypothyroidism [9]. The coexistence of these disorders may contribute to an elevated susceptibility to cardiovascular diseases (CVDs).

There exists empirical data suggesting the necessity of evaluating thyroid function in individuals diagnosed with metabolic syndrome, particularly those who have an elevated risk for cardiovascular disease (CVD). Obesity has been found to induce changes in thyroid hormone levels, whereas subclinical hypothyroidism is associated with a reduced metabolic rate that can contribute to the development of obesity. The causal relationship between changes in thyroid hormone levels and obesity (metabolic syndrome) remains uncertain. The thyroid gland assumes a crucial function in the control of metabolism. Thyroid hormones exert various influences on glucose and lipid metabolism, control of blood pressure, and energy expenditure [10, 11]. Recent research investigations have revealed a positive correlation between the presence of hypothyroidism and subclinical hypothyroidism in individuals, and an elevated susceptibility to metabolic syndrome. There is a growing body of research indicating that thyroid dysfunction has an impact on lipid and glucose metabolism, blood pressure, and body weight. These effects are closely linked to several metabolic parameters and have the potential to contribute to the development or exacerbation of components associated with metabolic syndrome [12].

The objective of this study was to evaluate the occurrence and various clinical and epidemiological characteristics associated with thyroid dysfunction (TD) among Indian patients who have been diagnosed with metabolic syndrome (MetS).

Methods

The study was conducted in the Department of General Medicine for the period of 1 year. In this study, we had enrolled 300 patients with MetS.

Inclusion & exclusion criteria

Patients aged 18 to 65 years, with an established diagnosis of MetS based on the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III criteria (with modified waist), with or without known TD, were invited to participate in the study during their routine clinical visit to the endocrinologists, gastroenterologists, and/or hepatologists. Pregnant patients or patients with a history of jejunoileal bypass, biliopancreatic diversion, extensive small bowel resection, total parenteral nutrition, any forms of chronic liver disease, hepatocellular carcinoma, patients on weight loss therapies or steatogenic drugs, and known HIV-positive cases were excluded from the study.

Methodology

At the screening visit, the following data were collected in the case report forms: demographics, anthropometric measurements, significant medical (including FPG, serum TG, and HDL-C values from patients' medical records) and surgical history, family history, lifestyle parameters, history of consumption of any obesogenic medicines, vital signs, and details of physical examination.

After obtaining an informed signed consent to participate in the study, the eligible patients from the screening visit were requested to visit the clinic after an overnight fast within 3-10 days of consenting. At this visit (visit 1), abdominal ultrasound examination (USG) was performed in patients who did not consume alcohol or consumed less than 20 g of alcohol per day and had not received corticosteroids, amiodarone, or tamoxifen. Blood samples were collected for assessment of hemogram, coagulogram (activated partial thromboplastin time, thrombin time, and prothrombin time), plasma insulin, plasma glucose, lipid profile (TG, total cholesterol (TC), HDL-C, and low-density lipoprotein cholesterol (LDL-C)), and thyroid function (free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH)). The fasting plasma glucose and plasma insulin were used for the calculation of homeostatic model assessment-established IR (HOMA-IR). The patients were followed up for a mean of one year to check for new diagnoses of TD.

The primary endpoint was the prevalence of TD among patients with MetS. Other endpoints included the percentage of patients with hyperthyroidism, subclinical hyperthyroidism, hypothyroidism, and subclinical hypothyroidism and percentage of patients with TD with respect to individual components of MetS (waist circumference, TG, HDL-C, SBP, DBP, and fasting glucose) and IR (HOMA − IR > 1 64).

Statistical Analysis

All statistical analyses were performed using SAS® version 9.2 (SAS Institute Inc., USA). The prevalence of TD in MetS patients was calculated as a number and percentage with 95% CI.

Results

Table 1: Demographics and baseline characteristics of 432 patients with metabolic syndrome

Parameter	Age ≤ 45 y (N = 100)	Age > 45 y (N = 200)	Total (N = 300)
Age in years			
Mean (SD)	38.2 (6.04)	56.4 (5.55)	48.2 (10.90)
Range	21.0-45.0	46.0-65.0	21.0-65.0
Gender			
Women, N (%)	60 (60%)	110 (55%)	170 (56.66%)
Men, N (%)	40 (40%)	90 (45%)	130 (43.34%)
Height in cm, mean (SD)	164.0 (9.01)	161.9 (8.52)	162.8 (8.72)
Weight in kg, mean (SD)	79.4 (13.13)	75.8 (12.29)	77.3 (12.75)
Waist circumference in cm, mean (SD)	98.5 (9.41)	98.7 (9.92)	98.6 (9.70)
Hip circumference in cm, mean (SD)	106.3 (11.07)	104.7 (11.14)	105.4 (11.13)

In this study, we had enrolled 300 patients with MetS. There was female dominance over men in both the groups. Mean height was 164.0±9.01 and 161.9±8.52 in the groups respectively. Mean weight was 79.4±13.13 and 75.8±12.29 in the groups respectively.

Table 2: Percentage prevalence of different grades of thyroid dysfunction

Classification of TD	MetS patients (N = 300) N (%)
Hypothyroidism	60 (20)
New overt hypothyroidism	6 (2)
New subclinical hypothyroidism	30 (10)
Hyperthyroidism	6 (2)
New overt hyperthyroidism	0
New subclinical hyperthyroidism	3 (1)
Total number of TD patients	90 (30)

Of the 300 MetS patients, hypothyroidism was reported in 60 (20%) patients and overt hyperthyroidism in 6 (2%) patients.

Discussion

Metabolic syndrome encompasses a cluster of physiological disorders, including obesity, hypertension, dyslipidemia characterized by higher triglyceride levels and low high-density lipoprotein levels, as well as elevated fasting blood glucose levels. Individuals diagnosed with metabolic syndrome have an elevated susceptibility to the development of diabetes and cardiovascular ailments in subsequent periods. Thyroid dysfunction frequently occurs in individuals diagnosed with metabolic syndrome. The incidence of thyroid dysfunction among individuals diagnosed with metabolic syndrome has been investigated in many studies undertaken in India, Nepal, Middle Eastern countries, and numerous African nations, with rates ranging from 21% to 51% [13-16]. Metabolic syndrome has associations with both endocrine and non-endocrine illnesses, hence giving rise to extensive ramifications. The clinical recognition of alterations in thyroid functioning, despite being widely acknowledged, remains inconsistent in the context of metabolic syndrome [17]. It is well accepted that the pathophysiology of Metabolic Syndrome (MetS) is influenced by oxidative stress, chronic inflammation, and angiogenesis [18]. The key constituents of Metabolic Syndrome (MetS), such as hyperglycemia and inflammation, lead to an elevation in the generation of reactive oxygen species (ROS), which subsequently causes an escalation in oxidative stress accompanied by the excessive activation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase [19, 20]. The presence of a hypermetabolic state in individuals with hyperthyroidism has been seen to potentially enhance the generation of free radicals inside mitochondria, leading to alterations in the antioxidant defence system. The presence of oxidative stress in individuals with hypothyroidism can be attributed to a diminished ability of the antioxidative defense system.

In this research endeavour, a total of 300 individuals diagnosed with Metabolic Syndrome (MetS) were included as participants. In both groups, women exhibited control over males. The mean height in the groups was 164.0±9.01 and 161.9±8.52, respectively. The mean weight in the groups was 79.4±13.13 and 75.8±12.29, respectively. Among the cohort of 300 patients diagnosed with Metabolic Syndrome (MetS), a total of 60 individuals (20%) were found to have hypothyroidism, whereas 6 patients (2%) had overt hyperthyroidism. The relatively lower prevalence of subclinical hypothyroidism cases seen in our study may be attributable to the substantial inclusion of patients with preexisting hypothyroidism (17.5%), who were already receiving levothyroxine medication. The cumulative prevalence of hypothyroidism, including both pre-existing cases at baseline (17.5%) and newly diagnosed cases of overt hypothyroidism (2%) and subclinical hypothyroidism (10%), was determined to be 25.70%. Consistent with our research findings, other Indian studies have also revealed a comparable incidence of hypothyroidism in the population with Metabolic Syndrome (MetS), namely Kota *et al*. (26%) [21].

In the present investigation, it was shown that females diagnosed with Metabolic Syndrome (MetS) had a greater prevalence of Thyroid Dysfunction (TD) as compared to their male counterparts. This finding aligns with previous research indicating a higher frequency of thyroid dysfunction in women compared to males within the context of metabolic syndrome [16, 22, 23]. Individuals in the older age bracket, specifically those aged 45 years and above, of both genders had a greater prevalence of TD. The findings of our study align with previous research, which also observed a trend of higher TD with advancing age in both males and females [23, 24]. Therefore, it is plausible that age and gender may serve as noteworthy risk factors for TD in patients with Metabolic Syndrome (MetS), thereby necessitating a comprehensive assessment of clinical and laboratory parameters within these specific cohorts. The present study examined the components of metabolic syndrome (MetS) in

patients diagnosed with type 2 diabetes (TD). The detected MetS components were elevated waist circumference, decreased high-density lipoprotein cholesterol (HDL-C) levels, increased homeostatic model assessment of insulin resistance (HOMA-IR), elevated systolic and diastolic blood pressure, elevated fasting glucose levels, and elevated triglyceride (TG) levels. A greater percentage of females had waist circumference measurements exceeding the established threshold (>80 cm) in comparison to males. While additional studies have also documented a correlation between thyroid dysfunction (TD) and various components of metabolic syndrome (MetS), the validity of this link remains a subject of ongoing debate. The findings of a study conducted in Nigeria revealed a substantial association between Metabolic Syndrome (MetS) and elevated levels of Free Thyroxine (FT4) [25]. The study conducted by Kota *et al*. revealed a noteworthy correlation between subclinical hypothyroidism and metabolic syndrome (MetS) in Indian patients. Specifically, the researchers observed a link between thyroid-stimulating hormone (TSH) levels and total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein cholesterol (HDL-C) levels [21]. It is important to acknowledge that the majority of research investigating the association between thyroid dysfunction (TD) and components of metabolic syndrome (MetS) have mostly concentrated on subclinical hypothyroidism. Moreover, it is important to acknowledge that the occurrence of thyroid dysfunction (TD) in individuals with metabolic syndrome (MetS) and its association with its components might differ depending on several factors such as geographical location, age, gender, dietary habits, genetic predisposition, and environmental influences [24, 26, 27].

Conclusion

Thyroid dysfunction is a significant factor to consider as a potential consequence among those with metabolic syndrome. Numerous investigations have established that there is a higher prevalence of thyroid hormone abnormalities in females compared to males. The incidence of thyroid dysfunction in individuals diagnosed with metabolic syndrome (MetS) was found to be substantial, suggesting a potential relationship between thyroid function and MetS. The findings derived from the current investigation will contribute to the establishment of a link between thyroid dysfunction (TD) and metabolic syndrome (MetS). The timely identification of thyroid dysfunction (TD) in individuals with metabolic syndrome (MetS) would facilitate the implementation of early therapies with suitable lifestyle modification regimens, where needed, to alter the progression of the condition. Nevertheless, it is necessary to conduct future prospective studies with a substantial sample size in order to assess the effectiveness of TD treatment in terms of reducing MetS and its associated components.

Conflict of Interest

Not available

Financial Support

Not available

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