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PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN PATIENTS WITH METABOLIC SYNDROME-A CROSS-SECTIONAL STUDY

Original Article

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ABSTRACT

Background: Subclinical hypothyroidism (SCH), defined by elevated thyroid-stimulating hormone (TSH) with normal free thyroxine, is increasingly recognized for its metabolic implications. Metabolic syndrome (MetS), a cluster of cardiovascular risk factors, shares several pathophysiological overlaps with thyroid dysfunction. The coexistence of these two conditions may compound adverse health outcomes, yet local data remains limited.

Objective: To determine the prevalence of subclinical hypothyroidism among patients diagnosed with metabolic syndrome and assess associated demographic and clinical risk factors.

Methods: A cross-sectional study was conducted over eight months at a tertiary care hospital in Lahore, enrolling 270 adult patients with metabolic syndrome based on NCEP ATP III criteria. Data on demographics, anthropometric measurements, and lifestyle factors were collected. Biochemical assessments included fasting glucose, lipid profile, and thyroid function tests (TSH and free T4). Statistical analysis involved descriptive statistics, chi-square tests, and logistic regression using SPSS version 26, with p-values <0.05 considered significant.

Results: Subclinical hypothyroidism was observed in 21.5% of metabolic syndrome patients. It was significantly more prevalent among females. Patients with SCH exhibited higher rates of individual metabolic components including elevated triglycerides (81.0%), low HDL cholesterol (67.2%), and increased fasting glucose (84.5%) compared to euthyroid individuals. Female sex emerged as an independent predictor of SCH (OR: 1.84; 95% CI: 1.03–3.29).

Conclusion: Subclinical hypothyroidism is notably prevalent among patients with metabolic syndrome, with a greater clustering of metabolic abnormalities in affected individuals. These findings support routine thyroid screening in this high-risk group to facilitate early intervention and integrated management.

Keywords: Blood Glucose, Dyslipidemias, Female, Metabolic Syndrome, Obesity, Prevalence, Risk Factors, Thyrotropin, Thyroxine, Subclinical Hypothyroidism.

INTRODUCTION

Metabolic syndrome, a constellation of interrelated metabolic abnormalities including central obesity, insulin resistance, dyslipidemia, and hypertension, has emerged as a critical public health challenge due to its strong association with cardiovascular disease and type 2 diabetes mellitus (1). As the global prevalence of metabolic syndrome continues to rise, particularly in developing countries experiencing rapid urbanization and lifestyle transitions, researchers and clinicians are increasingly focused on identifying underlying or coexisting conditions that may further exacerbate health outcomes (2). Among these, subclinical hypothyroidism—characterized by elevated serum thyroid-stimulating hormone (TSH) levels with normal free thyroxine (fT4)—has gained attention as a potential endocrine disorder intricately linked with the metabolic syndrome spectrum. While overt hypothyroidism has long been associated with various metabolic disturbances, including dyslipidemia and weight gain, the implications of subclinical hypothyroidism are still being clarified (3,4). Existing literature suggests that even in the absence of overt symptoms, subclinical hypothyroidism may subtly contribute to metabolic dysfunction by altering lipid metabolism, increasing insulin resistance, and influencing vascular tone (5). Several population-based studies have indicated a possible higher prevalence of subclinical hypothyroidism among individuals with metabolic syndrome compared to the general population, raising questions about whether thyroid dysfunction may act as a driver or consequence of metabolic disturbances (6,7). However, these associations have not been uniformly observed across studies, and the directionality and causality of the relationship remain areas of debate.

Emerging evidence suggests that thyroid hormones play a significant role in energy homeostasis, glucose metabolism, and lipid regulation. Altered thyroid function—even within the subclinical range—can lead to modifications in basal metabolic rate and influence the expression of enzymes involved in lipid and carbohydrate metabolism (8). These changes may synergize with the pathophysiologic mechanisms already present in metabolic syndrome, such as chronic low-grade inflammation and endothelial dysfunction, thereby amplifying cardiovascular risk. Moreover, TSH itself has been proposed to exert direct effects on adipocytes and hepatic tissue, potentially exacerbating insulin resistance and fat accumulation independently of thyroid hormone levels (9,10). Understanding this interplay is crucial, especially in light of evidence suggesting that individuals with both metabolic syndrome and subclinical hypothyroidism may have an even higher risk of cardiovascular events than those with either condition alone (11). Despite these insights, a clear consensus on the prevalence and clinical relevance of subclinical hypothyroidism among patients with metabolic syndrome remains elusive, largely due to heterogeneity in study designs, population characteristics, and diagnostic thresholds. Some studies report prevalence rates of subclinical hypothyroidism in metabolic syndrome patients ranging from 10% to 25%, while others find no significant difference when compared to euthyroid individuals (12,13). Furthermore, the contribution of gender, age, body mass index, and other risk factors to the coexistence of these two conditions is not fully established. There is also limited data from specific populations and regions, which hinders the ability to make generalizable conclusions or develop region-specific screening guidelines.

This knowledge gap is particularly relevant in regions where both metabolic syndrome and thyroid disorders are increasingly prevalent, often due to shared risk factors such as sedentary lifestyles, dietary changes, and rising obesity rates. As such, there is a pressing need for targeted epidemiological studies that not only establish the prevalence of subclinical hypothyroidism among metabolic syndrome patients but also examine potential predictive factors and demographic correlations. Such studies can inform early detection strategies, promote holistic approaches to metabolic health, and potentially guide therapeutic decisions, such as whether thyroid hormone replacement is beneficial in this subgroup. In light of these considerations, the present study seeks to determine the prevalence of subclinical hypothyroidism in individuals diagnosed with metabolic syndrome and to assess the associated risk factors within this population. By elucidating this relationship through a cross-sectional analysis, the study aims to contribute meaningful data to the ongoing discourse and support more comprehensive management of metabolic health.

METHODS

This cross-sectional study was conducted over a period of eight months at a tertiary care hospital in Lahore with the objective of determining the prevalence of subclinical hypothyroidism in individuals diagnosed with metabolic syndrome and assessing associated risk factors. The research employed a hospital-based, observational design, which allowed for the evaluation of a representative population of patients routinely presenting for evaluation and management of metabolic disorders. Participants were recruited consecutively from the outpatient department of internal medicine. The sample size was calculated using a prevalence estimation formula for cross-sectional studies, assuming an expected prevalence of subclinical hypothyroidism in metabolic syndrome to be approximately 20%, with a 95% confidence interval and a 5% margin of error. Based on this assumption, the required sample size was calculated to be

246 individuals (2,3). To account for possible dropouts or exclusions due to incomplete data, the final target sample was adjusted to 270 participants. Inclusion criteria comprised adult patients aged between 18 and 65 years, of both sexes, who fulfilled the diagnostic criteria for metabolic syndrome according to the revised National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines. Specifically, the diagnosis required the presence of at least three of the following: waist circumference >102 cm in males or >88 cm in females, triglycerides ≥150 mg/dL, HDL cholesterol <40 mg/dL in males or <50 mg/dL in females, blood pressure ≥130/85 mmHg or current use of antihypertensive medication, and fasting blood glucose ≥100 mg/dL or known type 2 diabetes mellitus. Exclusion criteria included patients with previously diagnosed thyroid disorders, those on medications affecting thyroid function (e.g., amiodarone, lithium), pregnant women, individuals with acute or chronic systemic illnesses (such as chronic kidney disease, liver dysfunction, or malignancy), and those who declined participation.

Data collection involved a structured interview followed by clinical examination and biochemical analysis. Participants' demographic information, including age, sex, body mass index (BMI), smoking status, physical activity, dietary habits, and relevant medical history, were documented. Anthropometric measurements were taken by trained staff using standardized protocols. Blood pressure was measured using a calibrated sphygmomanometer after the participant had rested for at least five minutes in a seated position. Venous blood samples were drawn after an overnight fast of 8 to 12 hours. Laboratory assessments included fasting plasma glucose, lipid profile (total cholesterol, HDL, LDL, triglycerides), serum TSH, and free T4. Thyroid function tests were performed using a chemiluminescence immunoassay technique, which is widely validated for accurate assessment of subclinical hypothyroidism (14,15). Subclinical hypothyroidism was defined as a serum TSH level above the upper reference limit (typically >4.5 mIU/L) with a normal free T4 level.

All data were anonymized and entered into a secure database for analysis. Statistical analysis was conducted using SPSS version 26. Continuous variables such as age, BMI, blood pressure, glucose, and lipid levels were presented as means and standard deviations. Categorical variables, including sex, presence of subclinical hypothyroidism, and individual components of metabolic syndrome, were expressed as frequencies and percentages. The normality of continuous data was confirmed using the Kolmogorov-Smirnov test. Differences between groups (i.e., those with and without subclinical hypothyroidism) were assessed using independent t-tests for continuous variables and chi-square tests for categorical variables. Logistic regression analysis was performed to identify independent predictors of subclinical hypothyroidism among metabolic syndrome patients, with odds ratios and 95% confidence intervals reported. A p-value of less than 0.05 was considered statistically significant. Prior to the commencement of the study, ethical approval was obtained from the Institutional Review Board (IRB) of the hospital. All participants were provided with verbal and written information about the study in their native language and were required to give written informed consent before inclusion. Confidentiality and the right to withdraw at any stage were assured to all participants in accordance with the principles of the Declaration of Helsinki. By employing rigorous inclusion criteria, standardized measurement tools, and validated laboratory techniques, this study aimed to ensure high internal validity. The findings are expected to contribute meaningful insight into the burden of subclinical hypothyroidism in individuals with metabolic syndrome and to support improved screening and management practices in similar clinical settings.

RESULTS

Out of the total 270 participants recruited for the study, 122 (45.2%) were male and 148 (54.8%) were female. The mean age of the sample population was 48.3 ± 9.2 years, and the average BMI was 29.7 ± 3.5 kg/m². The majority of patients had central obesity, with a mean waist circumference of 102.4 ± 8.6 cm. Smokers comprised 32.6% of the study cohort. Among all participants with metabolic syndrome, 58 individuals (21.5%) were found to have subclinical hypothyroidism, while 212 (78.5%) were euthyroid. This distribution is illustrated in Figure 1 ("Thyroid Status Distribution"). When stratified by metabolic syndrome components, those with subclinical hypothyroidism had a consistently higher prevalence of all measured components. Specifically, high waist circumference was observed in 93.1% of patients with subclinical hypothyroidism compared to 87.7% of those without. Similarly, high triglycerides were present in 81.0% versus 72.2%, low HDL in 67.2% versus 54.2%, hypertension in 77.6% versus 67.0%, and elevated fasting glucose in 84.5% versus 75.9%, respectively. These comparisons are visually summarized in Figure 2 ("Comparison of Metabolic Components by Thyroid Status"). Logistic regression analysis identified female sex as a statistically significant independent predictor of subclinical hypothyroidism, with an adjusted odds ratio (OR) of 1.84 (95% CI: 1.03–3.29; p = 0.038). Other factors such as age >50 years, BMI ≥30, smoking status, and physical inactivity were not found to be significantly associated with increased odds of subclinical hypothyroidism in this cohort. The results from this cross-sectional analysis underscore a notably high burden of subclinical hypothyroidism among individuals with metabolic syndrome and suggest a stronger clustering of metabolic abnormalities in this subgroup, particularly among females.

Table 1: Demographic Characteristics of Study Participants

Variable	Mean ± SD / Percentage
Age (years)	48.3 ± 9.2
Gender	
Male (%)	122 (45.2%)
Female (%)	148 (54.8%)
BMI (kg/m²)	29.7 ± 3.5
Waist Circumference (cm)	102.4 ± 8.6
Smokers (%)	88 (32.6%)

Table 2: Thyroid Status Distribution among Participants

Thyroid Status	Number of Patients (%)
Subclinical Hypothyroidism	58 (21.5%)
Euthyroid	212 (78.5%)

Table 3: Metabolic Syndrome Components in Patients with and without Subclinical Hypothyroidism

Component	With SCH (n=58)	Without SCH (n=212)
High Waist Circumference	54 (93.1%)	186 (87.7%)
High Triglycerides	47 (81.0%)	153 (72.2%)
Low HDL	39 (67.2%)	115 (54.2%)
Hypertension	45 (77.6%)	142 (67.0%)
High Fasting Glucose	49 (84.5%)	161 (75.9%)

Table 4: Logistic Regression Analysis of Risk Factors for Subclinical Hypothyroidism

Risk Factor	Adjusted OR (95% CI)	p-value
Female Sex	1.84 (1.03–3.29)	0.038
Age > 50	1.57 (0.89–2.76)	0.114
BMI ≥ 30	1.42 (0.77–2.61)	0.253
Smoking	0.93 (0.49–1.78)	0.830
Physical Inactivity	1.26 (0.68–2.32)	0.467

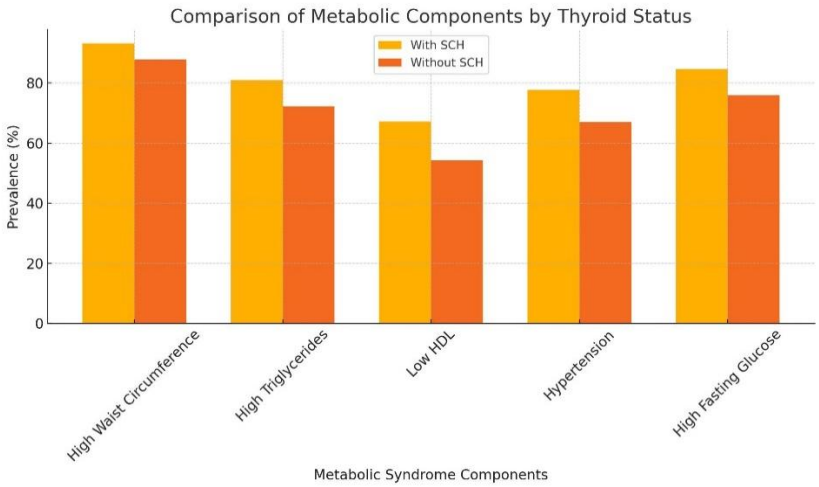

Figure 1 Comparison of Metabolic Components by Thyroid Status

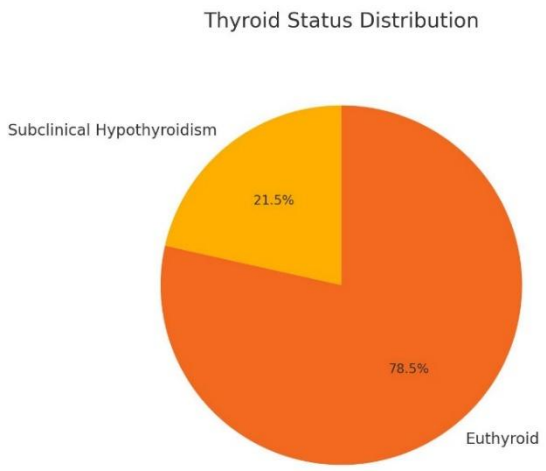

Figure 2 Thyroid Status Distribution

DISCUSSION

The findings of the present study reveal a significant prevalence of subclinical hypothyroidism (SCH) among individuals diagnosed with metabolic syndrome (MetS), with a frequency of 21.5%. This observation aligns with several recent studies conducted in diverse geographic and ethnic populations, reinforcing the notion of a substantive link between these two commonly encountered clinical entities. For instance, a study reported a SCH prevalence of 30.1% among MetS patients, also observing a predominance among females and individuals in their 40s (16). These findings suggest that even in the absence of overt hypothyroidism, subtle thyroid dysfunction may contribute to or coexist with the pathophysiological mechanisms underlying metabolic syndrome. Elevated TSH levels, despite normal circulating thyroid hormones, may influence adiposity, lipid metabolism, and insulin sensitivity. Notably, components such as high triglycerides, low HDL cholesterol, elevated fasting glucose, and increased waist circumference were more prevalent among SCH patients in this study. Similar metabolic derangements have been documented in various cross-sectional studies, underscoring the role of thyroid function in metabolic regulation (17-19). Importantly, female sex emerged as a significant independent predictor of SCH in the current cohort. This is consistent with broader epidemiological data suggesting that women are disproportionately affected by thyroid disorders, particularly in middle age (20). Estrogen-related hormonal modulation and autoimmune susceptibility may underlie this sex-based disparity. Furthermore, although age and BMI were not statistically significant predictors in this study, prior investigations have identified advancing age and obesity as risk enhancers for SCH in the MetS population (21).

Despite its cross-sectional design, which precludes the establishment of causality, this study adds to the accumulating evidence that metabolic syndrome and subclinical hypothyroidism are intertwined conditions that may potentiate each other's clinical impact. The observed clustering of metabolic abnormalities in SCH patients supports the hypothesis that thyroid dysfunction, even at a subclinical level, may aggravate cardiovascular risk profiles among patients with MetS (22,23). This study is strengthened by a well-defined population, standardized measurement protocols, and robust statistical analysis. However, some limitations must be acknowledged. Being a single-center study, generalizability to other populations is limited. Moreover, factors such as dietary iodine intake, thyroid autoantibody status, and longitudinal follow-up were not included, which could have provided further insight into etiological mechanisms and progression. Future studies incorporating a larger, multicenter cohort and prospective design are warranted to clarify whether SCH contributes causally to the development of MetS or merely coexists due to overlapping risk factors. Further exploration of whether levothyroxine therapy in MetS patients with SCH mitigates metabolic risk also remains an open and relevant clinical question. In conclusion, this study reinforces the high prevalence of subclinical hypothyroidism in individuals with metabolic syndrome and highlights a greater burden of metabolic abnormalities in affected patients. These findings support the inclusion of thyroid function screening as part of the metabolic syndrome management protocol, particularly in women and in those with multiple metabolic risk factors.

Conclusion

This study establishes a significant prevalence of subclinical hypothyroidism among individuals with metabolic syndrome, particularly in females, and highlights a stronger clustering of metabolic risk factors in this group. These findings underscore the need for routine thyroid function screening in patients with metabolic syndrome to facilitate early detection and integrated management strategies that may reduce long-term cardiovascular risk.

AUTHOR CONTRIBUTION

Author	Contribution
Bilal Khan*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Zahid Hussain	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
M. Hamza Ijaz	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Syeda Nazish Sohaib	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Syeda Fareeha Tauheed	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Sohail Nasir	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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