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**Original Research Article**

# Metabolic Syndrome and its Components as Risk Factors for Benign Thyroid Nodules

Dr. Tasnim Tabassum Progga[1]*, Dr. Shahla Shobnom[2], Dr. Sharmin Jahan[3], Dr. Salma Akter[4], Prof. Dr. Farhadul Hoque Mollah[5]

[1]Assistant Professor, Department of Biochemistry, Fazlur Rahman Medical College, Dhaka, Bangladesh
[2]Consultant & Dermato Surgeon, Department of Dermatology & Venereology and Aesthetic Dermatology, Labaid Aesthetic & Laser Lounge, Dhaka, Bangladesh
[3]Assistant Professor, Department of Biochemistry, Gazi Medical College, Khulna, Bangladesh
[4]Assistant Professor, Department of Biochemistry, Dhaka Medical College, Dhaka, Bangladesh
[5]Professor, Department of Biochemistry and Molecular Biology, Bangladesh Medical University, Dhaka, Bangladesh

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***Corresponding author:** Dr. Tasnim Tabassum Progga
Assistant Professor, Department of Biochemistry, Fazlur Rahman Medical College, Dhaka, Bangladesh

## Abstract

***Background:*** The rising global prevalence of both metabolic syndrome (MetS) and thyroid nodules (TN) suggests a potential pathophysiological link. This study aimed to investigate the association between MetS and its individual components with the presence of thyroid nodules. ***Methods:*** A cross-sectional analytical pilot study was conducted over six months. A total of 70 participants (35 with benign TN and 35 without benign TN), aged 18-75 years, were enrolled via purposive sampling. MetS was diagnosed according to standard criteria requiring ≥3 of the following: elevated waist circumference, high blood pressure, impaired fasting glucose (IFG), high triglycerides, or low HDL-cholesterol. Anthropometric measurements, blood pressure, thyroid ultrasonography, and fasting blood samples for glucose, lipids, and thyroid function tests (TSH, FT3, FT4) were obtained. According to the exclusion criteria, cases with malignant thyroid nodules were resected. In this study, as thyroid nodules, only benign thyroid nodules were considered. Data were analyzed using unpaired t-tests, chi-square tests, and multiple logistic regression. ***Results:*** The prevalence of MetS was significantly higher in the nodule group compared to the control group (68.57% vs. 40.00%, p=0.001). Participants with nodules had significantly higher mean values for waist circumference, systolic and diastolic blood pressure, and fasting plasma glucose (all p<0.05). Low HDL-cholesterol (82.9% vs. 37.1%, p=0.046), high blood pressure (51.4% vs. 17.1%, p=0.005), and IFG (48.6% vs. 25.7%, p=0.004) were significantly more prevalent in the nodule group. Multiple logistic regression confirmed MetS (OR=5.00, 95% CI: 2.48-8.60, p=0.001), along with age, SBP, FT3, and FT4, as independent risk factors for TN. ***Conclusion:*** Metabolic syndrome and several of its components are significantly associated with an increased risk of thyroid nodules, suggesting that metabolic health may play a crucial role in thyroid nodule pathogenesis. The sample size was very small due to the COVID-19 situation.

**Keywords:** Dyslipidemia, Metabolic syndrome, Risk factors, Thyroid function tests, Thyroid nodule, Ultrasonography, Waist circumference.



## INTRODUCTION

Thyroid nodules, defined as discrete lesions within the thyroid gland that are radiologically distinct from the surrounding parenchyma, represent a common clinical finding with a steadily increasing prevalence worldwide, largely attributable to the widespread use of high-resolution neck ultrasonography [1]. While the majority of nodules are benign, their clinical significance lies in the need to exclude malignancy and manage potential compressive symptoms or functional autonomy [2]. The etiopathogenesis of thyroid nodule formation is multifactorial, involving a complex interplay of genetic predisposition, environmental factors, and endogenous hormonal influences [3]. Established risk factors include female gender, advanced age, and a history of iodine deficiency or radiation exposure [4]. However, the sharp rise in prevalence suggests a strong influence from modifiable lifestyle and metabolic factors, prompting investigation into their specific roles. Parallel to the increase in thyroid nodules, the global incidence of

metabolic syndrome (MetS) has reached epidemic proportions. MetS is a clustering of cardiometabolic risk factors, including abdominal obesity, hypertension, dysglycemia, and dyslipidemia (elevated triglycerides and low high-density lipoprotein cholesterol) [5]. This syndrome is a well-established precursor to cardiovascular disease and type 2 diabetes mellitus, reflecting a state of chronic low-grade inflammation and insulin resistance (IR) [6]. The pathophysiological links between IR, chronic inflammation, and cellular proliferation provide a plausible biological basis for a connection between MetS and oncogenic processes, including those affecting the thyroid gland [7]. Emerging evidence over the past decade has begun to solidify the association between MetS and thyroid nodules. Several large-scale epidemiological studies have reported a higher prevalence and incidence of thyroid nodules in individuals with MetS compared to those without [8,9]. The components of MetS appear to contribute synergistically to this risk. For instance, insulin resistance, a core defect in MetS, may promote thyrocyte growth through the mitogenic effects of hyperinsulinemia and increased insulin-like growth factor-1 (IGF-1) activity [10]. Furthermore, abdominal obesity is associated with a state of adipokine dysregulation, characterized by increased leptin and decreased adiponectin, which can further stimulate proliferative and inflammatory pathways within the thyroid [11]. Hypertension and dyslipidemia have also been independently linked to nodular thyroid disease, potentially through mechanisms involving oxidative stress and endothelial dysfunction [12,13]. Despite the growing body of evidence, the independent contribution of each MetS component to thyroid nodule risk within specific populations warrants further investigation. Therefore, this cross-sectional study aims to evaluate the link between metabolic syndrome and its individual components with the presence of thyroid nodules in a clinical setting. We hypothesize that the presence of MetS is significantly associated with a higher risk of thyroid nodules, and that specific components, such as deglycation and dyslipidemia, are key drivers of this association.

## METHODOLOGY

**Study population:** This cross-sectional pilot study enrolled 70 participants, grouped into 35 with thyroid nodules and 35 without. Subjects were recruited from the Otolaryngology department outpatient clinic at Bangabandhu Sheikh Mujib Medical University (BSMMU).

**Inclusion criteria:** Participants aged 18 to 75 years, both male and female, were included in the study. Accompanying persons meeting the criteria were also eligible.

**Exclusion criteria:** Individuals were excluded for malignant thyroid nodules, pregnancy, lactation, smoking, alcohol use, pre-existing chronic diseases (renal, hepatic, cardiac), infection, inflammation, malignancy, history of thyroid surgery or radiation, and use of medications affecting thyroid function.

**Study procedure:** After ethical approval and obtaining informed consent, all subjects underwent thyroid ultrasonography for nodule diagnosis. Anthropometric measurements (weight, height, waist circumference) and blood pressure were recorded. Fasting blood samples were collected to analyze glucose, triglycerides, HDL-cholesterol, TSH, FT3, and FT4 using standard automated methods.

**Data analysis:** Data were analyzed using SPSS version 20. Continuous variables were expressed as mean ± SD and compared using the unpaired t-test. Categorical variables were compared with the chi-square test. A multiple logistic regression analysis was performed to identify independent risk factors. A p-value of $\leq 0.05$ was considered statistically significant.

## RESULT

The study comprised a total of 70 participants, equally divided into two groups: 35 with thyroid nodules and 35 without. The group with nodules had a mean age of 40.9 ± 11.24 years, which was significantly higher than the control group's mean age of 34.07 ± 7.96 years ($p = 0.009$). Regarding physical and metabolic parameters, significant differences were observed between the groups. Participants with nodules had a higher mean weight (68.30 ± 9.48 kg vs. 63.20 ± 7.55 kg, $p = 0.025$), larger waist circumference (90.19 ± 9.52 cm vs. 84.76 ± 8.00 cm, $p = 0.020$), and elevated systolic (124.00 ± 8.65 mmHg vs. 116.00 ± 6.94 mmHg, $p = 0.020$) and diastolic blood pressure (79.00 ± 8.75 mmHg vs. 73.67 ± 8.50 mmHg, $p < 0.001$). No significant difference was found in BMI between the groups ($p = 0.060$). A striking difference was observed in the prevalence of metabolic syndrome. The condition was present in 68.57% (n=24) of participants in the nodule group, compared to only 40.00% (n=14) in the control group, a difference that was statistically highly significant ($p = 0.001$). Analysis of the individual components of metabolic syndrome revealed that certain factors were markedly more common in those with nodules. Impaired fasting glucose was present in 48.6% of the nodule group versus 25.7% of the control group ($p = 0.004$). Similarly, hypertension was significantly more prevalent in the nodule group (51.4% vs. 17.1%, $p = 0.005$). The most pronounced difference was in the prevalence of low HDL-cholesterol, which was found in 82.9% of the nodule group compared to 37.1% of those without nodules ($p = 0.046$). In contrast, the prevalence of abdominal obesity and high triglycerides did not differ significantly between the two groups. Biochemically, the mean fasting plasma glucose level was higher in the nodule group (6.33 ± 1.64 mmol/L vs. 5.96 ± 2.11 mmol/L, $p = 0.043$). Thyroid function tests showed that while TSH levels were comparable, free thyroid hormone levels differed. The mean FT3 level was lower

in the nodule group (5.01 ± 0.88 pmol/L vs. 5.42 ± 0.70 pmol/L, p = 0.050), whereas the mean FT4 level was significantly higher (14.10 ± 1.96 pmol/L vs. 12.71 ± 2.40 pmol/L, p = 0.018). A multiple logistic regression analysis confirmed that after adjusting for other variables, metabolic syndrome itself was a strong, independent risk factor for thyroid nodules, with an odds ratio of 5.00. Additionally, age, systolic blood pressure, and the thyroid hormones FT3 and FT4 remained significantly and independently associated with the presence of nodules.

**Table 1: Baseline demographic and clinical characteristics of the study participants, stratified by thyroid nodule status (N=70)**

| Variable | With nodules (n=35) | Without nodules (n=35) | p-value |
|---|---|---|---|
| | Mean ± SD | | |
| Age (years) | 40.90 ± 11.24 | 34.07 ± 7.96 | 0.009 |
| Height (cm) | 159.50 ± 7.69 | 157.78 ± 5.33 | 0.320 |
| Weight (kg) | 68.30 ± 9.48 | 63.20 ± 7.55 | 0.025 |
| BMI (kg/m²) | 26.77 ± 2.83 | 25.43 ± 2.56 | 0.060 |
| Waist circumference (cm) | 90.19 ± 9.52 | 84.76 ± 8.00 | 0.020 |
| Systolic BP (mmHg) | 124.00 ± 8.65 | 116.00 ± 6.94 | 0.020 |
| Diastolic BP (mmHg) | 79.00 ± 8.75 | 73.67 ± 8.50 | <0.001 |

Abbreviation: SD, Standard Deviation; BMI, Body Mass Index; BP, Blood Pressure. *Data are presented as mean ± SD. P-values were calculated using the unpaired t-test. Bolded p-values indicate statistical significance (p ≤ 0.05)

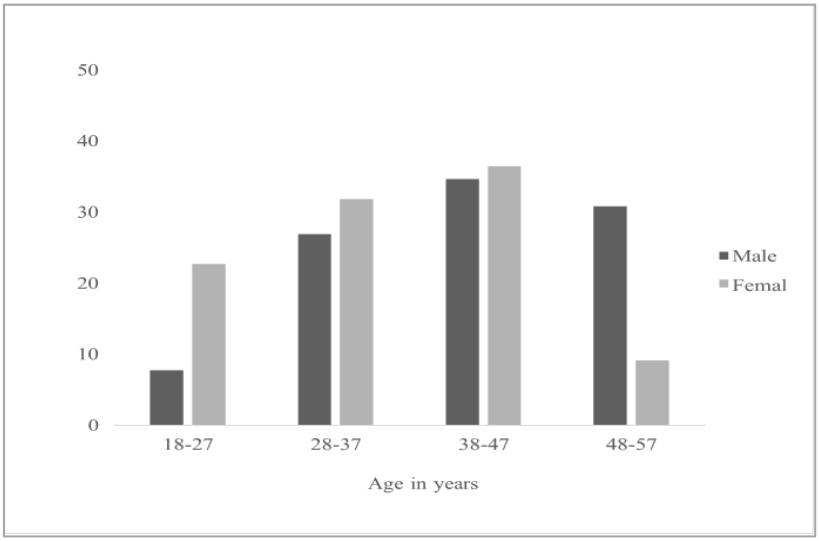


**Figure 1: Gender and age distribution of the total study population**

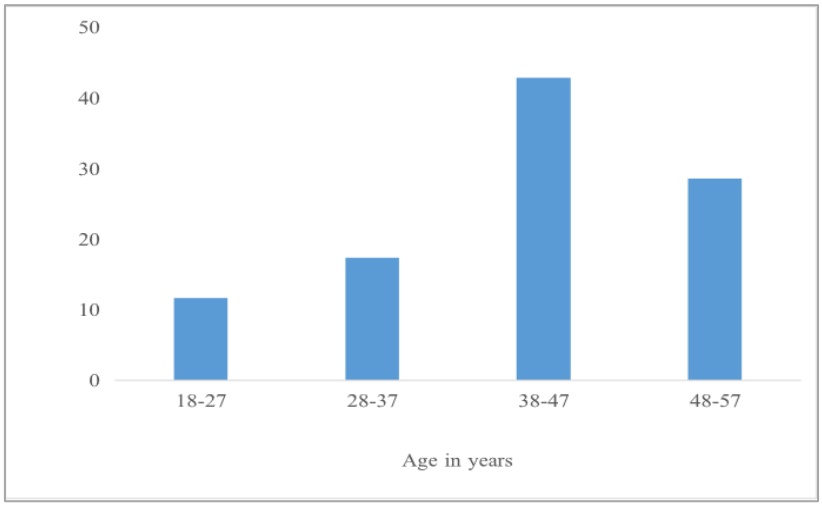


**Figure 2: Age-specific distribution of thyroid nodule prevalence in the study cohort**

**Table 2: Prevalence of metabolic syndrome in study participants with and without thyroid nodules. (N=70)**

| Metabolic syndrome | With nodules (n=35) | Without nodules (n=35) | p-value |
|---|---|---|---|
| | n (%) | | |
| Present | 24 (68.57) | 14 (40.00) | 0.001 |
| Absent | 11 (31.43) | 21 (60.00) | |
| **Total** | **35 (100)** | **35 (100)** | |

*Data presented as number of participants (n) and percentage (%). P-value was calculated using the Chi-square test. A p-value of ≤ 0.05 was considered statistically significant

**Table 3: Comparison of individual metabolic syndrome components (Categorical) between groups with and without thyroid nodules. (N=70)**

| Variable | Status | With nodules (n=35) | Without nodules (n=35) | p-value |
|---|---|---|---|---|
| | | n (%) | | |
| Abdominal obesity | Present | 24 (68.6) | 20 (57.1) | 0.458 |
| | Absent | 11 (31.4) | 15 (42.9) | |
| Impaired fasting glucose | Present | 17 (48.6) | 9 (25.7) | 0.004 |
| | Absent | 18 (51.4) | 26 (74.3) | |
| High blood pressure | Present | 18 (51.4) | 6 (17.1) | 0.005 |
| | Absent | 17 (48.6) | 29 (82.9) | |
| High triglycerides (TG) | Present | 13 (37.1) | 13 (37.1) | 1.000 |
| | Absent | 22 (62.9) | 22 (62.9) | |
| Low HDL-C | Present | 29 (82.9) | 13 (37.1) | 0.046 |
| | Absent | 6 (17.1) | 22 (62.9) | |

Abbreviation: HDL-C, High-Density Lipoprotein Cholesterol. *Data presented as number (n) and percentage (%). P-values were calculated using the Chi-square test. Bolded p-values indicate statistical significance (p ≤ 0.05)

**Table 4: Comparison of continuous metabolic and thyroid function parameters between study groups. (N=70)**

| Variable | With nodules (n=35) | Without nodules (n=35) | p-value |
|---|---|---|---|
| | Mean ± SD | | |
| Waist circumference (cm) | 90.15 ± 9.37 | 84.76 ± 7.99 | 0.019 |
| Systolic BP (mmHg) | 123.55 ± 8.87 | 116.33 ± 6.94 | 0.016 |
| Diastolic BP (mmHg) | 78.39 ± 9.25 | 73.67 ± 8.50 | 0.051 |
| Fasting plasma glucose (mmol/L) | 6.33 ± 1.64 | 5.96 ± 2.11 | 0.043 |
| Triglycerides (mg/dL) | 156.74 ± 100.4 | 131.73 ± 63.83 | 0.252 |
| HDL-C (mg/dL) | 37.10 ± 6.52 | 39.07 ± 8.57 | 0.077 |
| TSH (mIU/L) | 2.13 ± 1.68 | 2.30 ± 2.99 | 0.676 |
| FT3 (pmol/L) | 5.01 ± 0.88 | 5.42 ± 0.70 | 0.050 |
| FT4 (pmol/L) | 14.10 ± 1.96 | 12.71 ± 2.40 | 0.018 |

*Abbreviations: SD, Standard Deviation; BP, Blood Pressure; HDL-C, High-Density Lipoprotein Cholesterol; TSH, Thyroid-Stimulating Hormone; FT3, Free Triiodothyronine; FT4, Free Thyroxine. **Data are presented as mean ± SD. P-values were calculated using the unpaired t-test. Bolded p-values indicate statistical significance (p ≤ 0.05)

**Table 5: Multiple logistic regression analysis of factors associated with thyroid nodule presence. (N=70)**

| Variable | p-value | Odds Ratio | 95% CI for OR |
|---|---|---|---|
| Age (years) | 0.037 | 0.749 | 0.570 - 0.983 |
| BMI (kg/m²) | 0.077 | 2.159 | 0.919 - 5.075 |
| Waist circumference (cm) | 0.085 | 1.188 | 0.977 - 1.444 |
| Systolic BP (mmHg) | 0.019 | 0.478 | 0.258 - 0.886 |
| Diastolic BP (mmHg) | 0.084 | 1.233 | 0.972 - 1.564 |
| Fasting plasma glucose (mmol/L) | 0.965 | 0.976 | 0.335 - 2.849 |
| Triglycerides (mg/dL) | 0.585 | 0.996 | 0.980 - 1.011 |
| HDL-C (mg/dL) | 0.184 | 1.134 | 0.942 - 1.364 |
| TSH (mIU/L) | 0.780 | 0.893 | 0.403 - 1.979 |
| FT3 (pmol/L) | 0.007 | 2.15 | 4.320 - 7.340 |
| FT4 (pmol/L) | 0.004 | 0.385 | 0.203 - 0.731 |

| Variable | p-value | Odds Ratio | 95% CI for OR |
|---|---|---|---|
| Metabolic syndrome (Present) | 0.001 | 5 | 2.475 - 8.600 |

Abbreviations: BMI, Body Mass Index; BP, Blood Pressure; HDL-C, High-Density Lipoprotein Cholesterol; TSH, Thyroid-Stimulating Hormone. *The dependent variable was the presence of thyroid nodules. Metabolic Syndrome was included as a dichotomous variable; all other variables were included as continuous variables. Bolded p-values indicate statistical significance ($p \leq 0.05$)

## DISCUSSION

This cross-sectional study demonstrates a significant and independent association between metabolic syndrome (MetS) and the presence of thyroid nodules. Our key finding is that individuals with thyroid nodules exhibited a markedly higher prevalence of MetS (68.57%) compared to those without nodules (40.00%). This result aligns with a growing body of evidence from various populations, reinforcing the concept that metabolic dysregulation plays a critical role in thyroid nodular pathogenesis [9,14]. The odds of having a thyroid nodule were five times higher in participants with MetS, even after adjusting for other variables, underscoring MetS as a potent cluster of risk factors. The analysis of individual MetS components revealed that not all contribute equally to the risk. Impaired fasting glucose (IFG) and high blood pressure were significantly more prevalent in the nodule group. The link with IFG supports the central hypothesis that insulin resistance (IR), a cornerstone of MetS, is a key driver. Hyperinsulinemia may promote thyrocyte proliferation directly via insulin receptors or indirectly by increasing the bioactivity of Insulin-like Growth Factor-1 (IGF-1), a known mitogen for thyroid cells [10,15]. The strong association with hypertension is consistent with previous studies [12] and may be related to shared pathways involving chronic inflammation, oxidative stress, and endothelial dysfunction, which can create a pro-proliferative microenvironment [16]. A particularly striking finding was the high prevalence of low HDL-C in the nodule group (82.9%). While HDL is known for its anti-inflammatory and antioxidant properties, low levels may permit increased oxidative damage within the thyroid gland, facilitating nodule formation [13,17]. The fact that abdominal obesity and high triglycerides did not show a significant difference in the categorical analysis was unexpected, though the mean waist circumference was significantly higher in the nodule group. This suggests that the continuous burden of adiposity may be more relevant than a simple dichotomous classification in this context. Our findings on thyroid function parameters add a nuanced layer to the discussion. We observed a statistically significant elevation in FT4 and a lower level of FT3 in the nodule group, despite normal TSH levels. This altered thyroid hormone ratio could indicate alterations in peripheral deiodinase activity, potentially influenced by the underlying metabolic state [18]. Furthermore, in the regression model, both FT3 and FT4 emerged as independent factors, suggesting that subtle variations in thyroid hormone homeostasis, even within the normal range, may be intertwined with nodule development or represent a consequence of the nodular process itself [19]. The strengths of this study include its rigorous methodological design with well-characterized groups and comprehensive biochemical profiling. However, several limitations must be acknowledged. Firstly, the cross-sectional nature precludes the determination of causality; we can only identify associations. Secondly, the sample size, though adequate for primary comparisons, may limit the power for more complex subgroup analyses. Finally, the study was conducted at a single tertiary care center, which may affect the generalizability of the findings to the broader population. This study provides compelling evidence that metabolic syndrome and specific components—namely, dysglycemia, hypertension, and low HDL-C—are strongly associated with thyroid nodules. These findings highlight the importance of evaluating the metabolic status of patients presenting with thyroid nodules. Future prospective longitudinal studies are needed to establish a causal relationship and to explore the underlying molecular mechanisms connecting insulin resistance, dyslipidemia, and thyroid cell proliferation.

**Limitations:**

The main limitations of this study are its cross-sectional design, which prevents causal inference, and the relatively small sample size from a single center, which may limit the generalizability of the findings to broader populations. The sample size was also very small because of the COVID-19 situation.

## CONCLUSION

This study conclusively demonstrates a significant association between metabolic syndrome and thyroid nodules, identifying MetS as a strong independent risk factor. Key components, including impaired fasting glucose, hypertension, and low HDL-C, were significantly linked to nodule presence. These findings highlight the critical role of metabolic health in thyroid nodule pathogenesis. Clinicians should consider evaluating the metabolic status of patients with thyroid nodules, as managing MetS could be a potential preventive strategy.

**Recommendation:**

Future large-scale, longitudinal studies are recommended to establish causality. Screening for thyroid nodules should be considered in patients with metabolic syndrome. Conversely, individuals diagnosed with nodules may benefit from evaluation for underlying metabolic abnormalities to enable comprehensive management.

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