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Proportion and Covariates of Hypothyroidism Among Patients with Metabolic Syndrome Attending in Tertiary Care Hospital

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Abstract

Background: Hypothyroidism in patients with metabolic syndrome is associated with worse outcomes. However, this has not yet been adequately investigated in Bangladeshi people. ***Objective:*** To find out the proportion and covariates of hypothyroidism among patients with metabolic syndrome. ***Materials and methods:*** A hospital-based cross-sectional study was conducted with 323 patients from the Endocrinology and Allied Medicine Department at BIRDEM General Hospital. Patients with metabolic syndrome but no prior diagnosis of hypothyroidism were included. Detailed history, physical examinations, and thyroid function tests—Thyroid Stimulating Hormone (TSH), Free Thyroxine (FT4), and Anti-Thyroid Peroxidase Antibody (Anti-TPO Ab)—were performed. Subclinical hypothyroidism was defined as TSH >4.12 mIU/L and <10 mIU/L, while overt hypothyroidism was defined as TSH >10 mIU/L. Statistical analyses, including Chi-square tests, ANOVA, Pearson's correlation, and multiple linear regression, were conducted to explore associations between components of metabolic syndrome and thyroid dysfunction. **Results:** Out of the 323 participants, 62.8% were euthyroid, 28.5% had subclinical hypothyroidism, and 8.7% had overt hypothyroidism. Autoimmune hypothyroidism was confirmed in 31.6% of hypothyroid patients through elevated Anti-TPO Ab levels, a statistically significant finding. Hypothyroidism was significantly more prevalent in females and obese individuals. Significant positive correlations were observed between TSH and waist circumference (r=0.153), systolic blood pressure (r=0.271), and triglycerides (r=0.128), while FT4 showed negative correlations. Multiple linear regression indicated significant associations between waist circumference, fasting plasma glucose, and thyroid dysfunction. **Conclusion:** It was concluded that a higher proportion of metabolic syndrome cases were suffering from hypothyroidism. This necessitates that all MetS patients be screened for thyroid profile and autoimmune status and managed accordingly.

Keywords: Metabolic syndrome, Subclinical hypothyroidism, Overt hypothyroidism.

INTRODUCTION

Metabolic syndrome is a modern epidemic and is considered one of the most pressing public health issues of this century [1]. It is characterized by a cluster of conditions, including hypertension, dyslipidemia, hyperglycemia, and prothrombotic and proinflammatory states, all of which accelerate the atherogenic process in the body. The worldwide prevalence of metabolic syndrome in the adult population is increasing, with an estimated 20-25% of adults affected. In Bangladesh, a developing country experiencing rapid urbanization and economic growth, lifestyle changes have led to a significant increase in the prevalence of metabolic syndrome. According to the National Cholesterol Education Program (NCEP) ATP-III criteria, 41.1% of Asian Indians and 30% of the Bangladeshi population suffer from metabolic syndrome [2]. Individuals with metabolic syndrome are at a significantly higher risk of cardiovascular events, being twice as likely to die from cardiovascular causes and three times more likely to experience a heart attack or stroke compared to those

without the syndrome. Central to metabolic syndrome is insulin resistance, which is believed to be the underlying pathophysiological mechanism driving this cluster of risk factors. Obesity, particularly the accumulation of visceral fat, is closely linked to insulin resistance and is a key component of metabolic syndrome [3]. Excess visceral fat is strongly associated with insulin resistance compared to other adipose tissue compartments, and it contributes to the release of non-esterified fatty acids, which in turn leads to the accumulation of lipids in non-adipose tissues such as muscle and liver [4]. This ectopic lipid accumulation predisposes individuals to insulin resistance and dyslipidemia, further exacerbating the metabolic syndrome. Additionally, patients with metabolic syndrome are at an increased risk of developing type 2 diabetes mellitus, which complicates their health status even further.

Atherogenic dyslipidemia, a hallmark of metabolic syndrome, is characterized by a specific pattern of lipoprotein abnormalities, including elevated serum triglycerides, increased apolipoprotein B, an abundance of small, dense low-density lipoprotein (LDL) particles, and reduced levels of high-density lipoprotein cholesterol (HDL-C) [5]. These lipid abnormalities are highly atherogenic, contributing to the development and progression of cardiovascular disease. Metabolic syndrome is often treated as a discrete entity with a single underlying cause, primarily insulin resistance, which connects the various components of the syndrome. In addition to metabolic syndrome, hypothyroidism is another condition with significant metabolic implications. Hypothyroidism can manifest as either overt or subclinical, with subclinical hypothyroidism characterized by an elevated serum thyroid-stimulating hormone (TSH) level combined with a standard free thyroxine (FT4) level. This condition is typically diagnosed when thyroid function has been stable for several weeks or more, with no recent severe illness impacting the hypothalamic-pituitary-thyroid axis. Overt hypothyroidism, on the other hand, is diagnosed when TSH levels exceed 10 mIU/L in combination with a subnormal FT4 level [6]. Although data on the prevalence of hypothyroidism in Bangladesh are limited, a community-based study in Khulna found that 6.59% of the population had subclinical hypothyroidism, while 4.97% had overt hypothyroidism.

Hypothyroidism is known to cause a range of metabolic disturbances, including dyslipidemia, diastolic hypertension, endothelial dysfunction, and cardiovascular disease [7]. Research from neighboring countries, such as India and Nepal, has shown that subclinical hypothyroidism is significantly associated with metabolic syndrome, with a linear relationship observed between TSH levels and total cholesterol, triglycerides, LDL, and HDL cholesterol levels in patients with metabolic syndrome. However, there is a lack of data on the prevalence and impact of hypothyroidism among patients with metabolic syndrome in Bangladesh. Both metabolic syndrome and hypothyroidism are well-established precursors of atherogenic cardiovascular disease. Several studies have reported that insulin resistance plays a crucial role in the overlap between metabolic syndrome and hypothyroidism, further complicating the diagnosis and management of patients with both conditions [8]. Moreover, some reports suggest that even TSH levels within the normal reference range may be associated with metabolic syndrome and its components, indicating a broader relationship between thyroid function and metabolic health.

Thyroid hormones are critical regulators of metabolic pathways, particularly those related to resting energy expenditure. Consequently, obesity and thyroid function are often interrelated. Obesity itself can lead to alterations in thyroid hormone levels, such as increased TSH, without significant changes in triiodothyronine (T3) and thyroxine (T4) levels [9]. Subclinical hypothyroidism, characterized by a slow metabolism, can contribute to obesity, creating a complex interplay between these conditions. However, it remains unclear whether these changes in thyroid hormone levels are a cause or consequence of obesity and metabolic syndrome. The mechanism underlying normal T3 and T4 levels with elevated TSH in patients with metabolic syndrome is unclear. However, it has been hypothesized that metabolic syndrome is associated with insulin resistance due to defects in post-receptor signal transduction in target tissues. This mechanism might also apply to thyroid receptor resistance in obese patients [10]. In obese individuals, adipose tissue is insulin resistant, leading to increased levels of non-esterified fatty acids, which worsen insulin resistance in muscle and alter hepatic metabolism. Additionally, the adipose tissue in obesity exhibits abnormalities in the production of several adipokines, which may independently affect insulin resistance and increase the risk of atherosclerotic cardiovascular disease.

Given that both metabolic syndrome and hypothyroidism are independent risk factors for cardiovascular disease, patients suffering from both conditions may have an elevated risk of cardiovascular morbidity and mortality. Early detection and treatment of hypothyroidism in patients with metabolic syndrome could potentially reduce cardiovascular complications and improve overall quality of life [11]. This study aims to investigate the proportion and covariates of hypothyroidism among patients with metabolic syndrome in a Bangladeshi cohort, providing insights for better management of these interrelated conditions.

OBJECTIVES

General objective

- To find out the proportion and covariates of hypothyroidism among patients with metabolic syndrome.

Specific objectives

- To assess thyroid hormone (FT4, TSH) status in metabolic syndrome patients.
- To observe different clinical characteristics of hypothyroidism in patients diagnosed with metabolic syndrome.
- To determine socio-demographic features in patients with metabolic syndrome.
- To find out the association of anti-thyroid antibodies with different thyroid function categories.
- To evaluate the relationship between components of metabolic syndrome and thyroid hormone (FT4, TSH) levels.

MATERIALS AND METHODS

Study Design

This study was conducted as a hospital-based cross-sectional study aimed at assessing the prevalence and associated factors of hypothyroidism among patients with metabolic syndrome. The research was carried out over two distinct periods, from March 2018 to April 2020 and March 2023 to September 2023. The study involved patients attending both the outpatient and inpatient departments of the Endocrinology and Internal Medicine Department at BIRDEM General Hospital, Dhaka. Participants were selected based on their diagnosis of metabolic syndrome, with all individuals aged 18 years and older included, irrespective of their socioeconomic status.

Inclusion criteria

- Diagnosed patients with features of metabolic syndrome.
- Not known to have hypothyroidism before in patients with metabolic syndrome
- Age >18 years.

Exclusion criteria

- Pregnant women.
- Female patient taking oral contraceptive pill.
- The patient is taking medication for thyroid replacement, anti-thyroid drug, amiodarone, corticosteroid, and lithium and has a recent history of taking contrast media.
- Patient with secondary hypothyroidism or surgically removed thyroid gland.
- Severely ill patients (taking into account sick euthyroid syndrome, CKD, CLD)

Data Collection

Data was gathered using a semi-structured questionnaire that captured respondents' socio-demographic, clinical, and anthropometric information. The data collection involved direct interviews, thorough clinical examinations, and relevant laboratory investigations to obtain comprehensive details about each participant. Trained healthcare professionals conducted the interviews and examinations, ensuring consistency and accuracy in the data collection process. All information was documented meticulously to facilitate subsequent analysis. This approach ensured that the data collected was robust, reliable, and reflective of the study's objectives.

Data Analysis

Following data collection, the collected data were assessed for completeness, accuracy, and consistency before analysis was commenced. Data analysis was carried out by using SPSS version 25. Data presented as mean ± standard deviation (SD) or number (%) unless specified. The Chi-square test analyzed all categorical data. A one-way ANOVA test for continuous data analyzed significance levels. Pearson's correlation coefficient and multiple linear regression analysis evaluated the association of hypothyroidism with different components of metabolic syndrome at 95 % confidence intervals, and a level of $p<0.05$ was considered statistically significant.

Ethical Consideration

Ethical standards were strictly adhered to throughout the study. Informed consent was obtained from all participants, ensuring they knew their rights and the study's purpose. Confidentiality and anonymity were maintained, with personal data securely stored and accessed only by authorized personnel. The study complied with the Helsinki Declaration and received approval from the institutional review board. Participants were also informed of their right to withdraw without repercussions.

RESULTS

This hospital-based cross-sectional study was conducted in the Endocrinology and Internal Medicine department, enrolling patients from both outpatient and inpatient departments of BIRDEM General Hospital. A total of 323 patients were analyzed in the study after considering exclusion and inclusion criteria.

Table 1: Socio-demographic characteristics of the study participants (n=323)

Characteristics	Frequency	Percentage (%)
Age (in years)		
19-40	78	24.1
41-62	177	54.8
63-84	68	21.1
Mean ± SD	51.58 ± 12.80	

Characteristics	Frequency	Percentage (%)
Gender		
Male	102	31.6
Female	221	68.4
Level of education		
Graduate	127	39.3
Undergraduate	179	55.4
Illiterate	17	5.3
Occupation		
Govt. Employee	27	8.4
Housewife	182	56.3
Others	114	35.2

Table 1 shows that most study participants (177, 54.8%) were 41-62. The mean age of the participants was 51.58 years, with a SD of 12.80. Maximum participants (221, 68.4%) were female. The female ratio was 1:2.2. Most participants (179, 55.4%) were undergraduates. Maximum study participants (182, 56.3%) were homemakers.

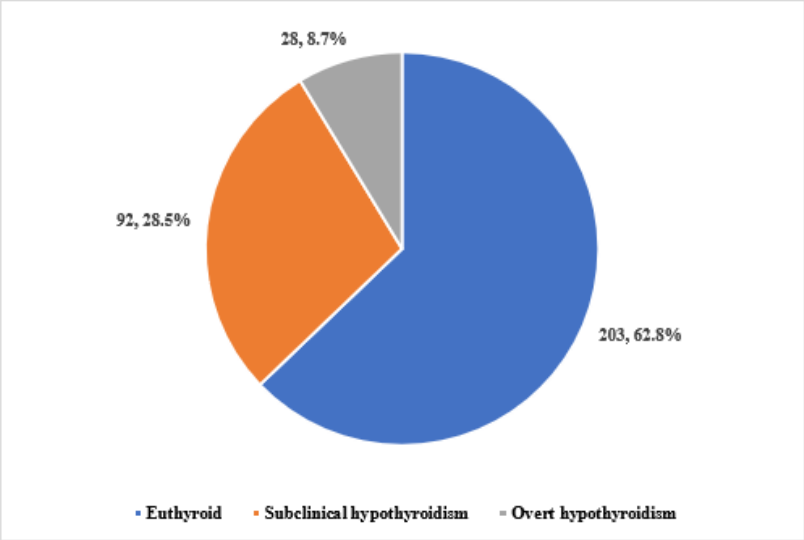

Figure 1: Thyroid dysfunction of the study participants (n=323)

Figure 1 shows that the majority of the participants (203, 62.8%) were euthyroid, followed by (92, 28.5%) who had SCH and (28, 8.7%) had overt hypothyroidism.

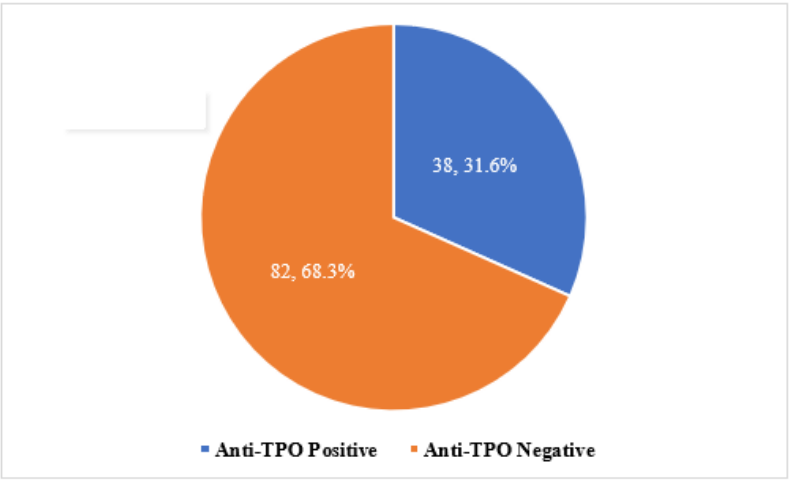

Figure 2: Distribution of hypothyroid patients according to Anti-thyroid peroxidase antibody (n=120)

Figure 2 shows that among the hypothyroid group, 31.6 % were Anti-TPO antibody positive, and 68.3% were Anti-TPO antibody negative.

Table 2: Comparison of components of metabolic syndrome, FT4, and 2TSH level among different thyroid dysfunction groups (n=323)

Variables		Euthyroid (n=203)	Subclinical (n=92)	Overt (n=28)	p-value
		Mean ± SD	Mean ± SD	Mean ± SD	
Waist circumference (cm)	Male	101.70±8.30	102.67±10.89	104.25±13.91	0.732
	Female	100.15±11.33	96.57±10.78	107.08±13.59	**0.001**^{s}
SBP (mmHg)		125.57±14.25	134.95±17.09	139.11±11.87	**<0.001**^{s}
DBP (mmHg)		77.29±10.43	80.11±11.07	83.21±9.36	**0.006**^{s}
FPG (mmol/l)		13.01±4.97	12.90±4.63	17.14±3.99	**<0.001**^{s}
TG (mg/dl)		191.01±37.33	226.08±86.35	212.61±91.36	**<0.001**^{s}
HDL (mg/dl)	Male	31.93±7.73	29.93±7.52	27.83±3.54	0.229
	Female	35.65±8.59	35.94±8.58	29.98±5.67	**0.014**^{s}
TSH		2.42±.78	6.74±1.61	18.59±7.69	**<0.001**^{s}
FT4		15.14±2.62	11.70±2.18	8.97±2.20	**<0.001**^{s}

Table 2 compares components of metabolic syndrome, FT4, and TSH levels among different thyroid dysfunction subgroups (euthyroid, subclinical, and overt) in patients with metabolic syndrome. For the waist circumference, females in the overt subgroup had a significantly higher mean than those in the subclinical and euthyroid subgroups (p=0.001). For SBP, DBP, and FPG, there was a significant difference among the three subgroups (p<0.001), with the overt subgroup having the highest mean. For TG, there were significant differences among the three subgroups (p<0.001), with the subclinical subgroup having the highest mean. For HDL-C, there was a significant difference among females in the three subgroups (p=0.014), with the overt subgroup having the lowest mean. There were significant differences among the three subgroups (p<0.001) for TSH, with the overt subgroup having the highest means. There were significant differences in FT4 levels (p<0.001), with the overt subgroup having the lowest mean.

Table 3: Correlation between components of metabolic syndrome with levels of FT4 and TSH among patients with metabolic syndrome (n=323)

Variables	TSH		FT4	
	r-coefficient	p-value	r-coefficient	p-value
Waist circumference (cm)	0.153**	**0.001**^{s}	-0.274**	**0.001**^{s}
SBP (mmHg)	0.271**	**0.001**^{s}	-0.177**	**0.001**^{s}
DBP (mmHg)	0.184**	**0.001**^{s}	-0.114*	**0.041**^{s}
FPG (mmol/l)	0.182**	**0.009**^{s}	-0.105	**0.058**^{ns}
TG (mg/dl)	0.249	**0.762**^{ns}	-0.128*	**0.021**^{s}
HDL-C (mg/dl)	-0.174	**0.169**^{ns}	0.091	**0.102**^{ns}

Table 3 shows the correlation between components of metabolic syndrome with levels of FT4 and TSH. The correlation coefficients indicate the strength and direction of the relationship between the two variables. A positive correlation coefficient indicates that as one variable increases, the other variable also tends to increase. A negative correlation coefficient indicates that the other variable tends to decrease as one variable increases. The p-values indicate the statistical significance of the correlation coefficients, and a value of less than 0.05 suggests that the correlation is statistically significant and not likely due to chance. The results show that waist circumference positively correlated with TSH (r=0.153, p=0.001) and a negative correlation with FT4 (r= -0.274, p=0.001). SBP had a positive correlation with TSH (r=0.271, p=0.001) and a negative correlation with FT4 (r= -0.177, p=0.001). DBP had a positive correlation with TSH (r=0.184, p=0.001) and a negative correlation with FT4 (r=-0.114, p=0.041). FPG positively correlated with TSH (r=0.182, p=0.009) but no significant correlation with FT4 (r=-0.105, p=0.058). TG had a significant negative correlation with FT4 (r=-0.128, p=0.021), and HDL-C had weak correlations with non-significant p-values for both TSH and FT4

Table 4: Factors influencing hypothyroidism in individuals with metabolic syndrome (n=323)

Parameters	Odds Ratio (OR)	95% CI for OR		P-value
		Lower	Upper	
Age (>45yrs vs <45yrs)	0.97	0.95	0.99	0.004^{s}
Gender (male vs female)	1.07	0.60	1.94	0.812^{ns}
BMI (overweight vs Obese)	1.04	0.98	1.02	0.612^{ns}
Family H/O thyroid disease	0.84	0.37	1.89	0.676^{ns}
Waist circumference	0.96	0.94	0.98	0.002^{s}
SBP	**1.06**	**1.04**	**1.08**	**0.001^{s}**
DBP	0.98	0.95	1.14	0.279^{ns}
FPG	0.98	0.94	1.04	0.646^{ns}
Total Cholesterol	1.03	0.99	1.01	0.480^{ns}
LDL	1.05	0.99	1.16	0.315^{ns}
TG	**1.01**	**1.02**	**1.12**	**0.004^{s}**
HDL-C	0.99	0.96	1.24	0.616^{ns}

Table 4 shows the factors influencing hypothyroidism in individuals with metabolic syndrome in multivariate binary logistic regression analysis and found SBP (OR-1.06), with a 95% confidence interval (CI) ranging from 1.04 to 1.08. An odds ratio of 1.06 suggests that patients with hypothyroidism are 1.06 times more likely to have a high SBP compared to the euthyroid group. Similarly, the TG level had significantly ($p<0.05$) increased 1.01 times, influencing hypothyroidism with 95% CI 1.02 to 1.12. However, other variables didn't exhibit any statistical significance in multivariate analysis.

DISCUSSION

The findings of this cross-sectional study revealed a significant prevalence of hypothyroidism among patients with metabolic syndrome, with 37.2% of participants diagnosed with some form of thyroid dysfunction. Among these, 28.5% were identified with subclinical hypothyroidism, while 8.7% were found to have overt hypothyroidism. These results align with existing literature, highlighting a considerable burden of thyroid dysfunction within this patient population. For instance, Bhaskar *et al.* reported a similar prevalence, with 35.2% of participants diagnosed with subclinical hypothyroidism and 13.9% with overt hypothyroidism [12,13]. This close resemblance in findings reinforces the notion that thyroid dysfunction is a common comorbidity in individuals with metabolic syndrome.

However, some studies have reported varying prevalence rates, which could be attributed to differences in sample size, study design, or the population studied. For example, Yadav *et al.* found a lower prevalence of subclinical hypothyroidism (12.5%) and overt hypothyroidism (10%) among their study participants [14]. This discrepancy might be explained by the differences in geographic location and genetic predispositions, as the study was conducted in a different region with a potentially different population structure and reported that 21% of their participants with metabolic syndrome had subclinical hypothyroidism. In comparison, 5% had overt hypothyroidism, which is slightly lower than our findings. These findings could be due to differences in diagnostic criteria, variations in iodine intake, and environmental factors that influence thyroid function in different populations.

Our study also observed that most participants were between 41 and 62 years old, with a mean age of 51.58. This is consistent with the findings of Bhaleghare *et al.*, who reported that most participants in their study were over 45 years old [15]. The mean age reported in a study was slightly higher at 52.6 years, reflecting similar demographic characteristics across different studies. The predominance of female participants in our study, with a female-to-male ratio of 2.2:1, is also consistent with other studies that report a higher prevalence of thyroid dysfunction in females. Reported female-to-male ratios of 1:0.78 and 1.94:1, respectively, underscoring the increased susceptibility of females to thyroid disorders, possibly due to hormonal differences.

The high prevalence of obesity among our participants, with 93.2% classified as obese and a mean BMI of 29.52 kg/m², further supports the strong association between metabolic syndrome and obesity. This finding is consistent with the study by El-Hay *et al.*, which reported a mean BMI of 31.36 kg/m² among their participants [16]. The association between obesity and thyroid dysfunction, particularly subclinical hypothyroidism, has been well-documented. While our study found that obese participants were more prone to develop subclinical hypothyroidism, reported that overweight participants were more likely to develop subclinical hypothyroidism. This difference could be attributed to the specific criteria used to define obesity and overweight in different studies and variations in body fat distribution among different populations.

Our study found that 31.6% of hypothyroid responders had autoimmune hypothyroidism, as indicated by raised anti-TPO antibody levels. This prevalence is lower than that reported in a study conducted at BIRDEM General Hospital by Selim *et al.*, where 68% of hypothyroid patients were autoimmune

positive [17]. The discrepancy in these findings could be due to differences in the study populations and the criteria used to define autoimmune hypothyroidism. Additionally, our study found that systolic and diastolic blood pressures were significantly higher in participants with hypothyroidism. This finding is consistent with those who reported significant associations between blood pressure and thyroid dysfunction. As hypothesized, this association's mechanism may involve the volume-dependent, low plasma renin activity mechanism of blood pressure elevation, particularly diastolic blood pressure.

Interestingly, our study revealed that participants with overt hypothyroidism had significantly higher waist circumferences, especially among females, compared to other metabolic syndrome indicators. This finding aligns with studies by Abha *et al.*, which also reported greater waist circumferences in women with thyroid dysfunction [18]. The association between waist circumference and thyroid dysfunction could be attributed to the role of thyroid hormones in regulating metabolism and fat distribution. Moreover, participants with hypothyroidism in our study had significantly higher fasting plasma glucose levels, particularly in the overt hypothyroid subgroup. This finding is supported by the study conducted, which reported that the risk of diabetes mellitus was increased by 2.29 times in individuals with subclinical hypothyroidism. The potential mechanisms for this association include reduced insulin sensitivity and altered glucose metabolism in hypothyroid states, as described by.

Our study also observed a significant positive correlation between TSH levels and waist circumference, systolic and diastolic blood pressures, and fasting plasma glucose levels, with a corresponding negative correlation between FT4 levels and these metabolic components. These findings are consistent with the study by He *et al.*, which also reported significant correlations between TSH levels and various components of metabolic syndrome [19]. The observed associations suggest a potential cardiovascular link between metabolic syndrome and hypothyroidism, as thyroid dysfunction may exacerbate the risk factors associated with cardiovascular disease. In addition to these findings, our study revealed a unique observation that FT4 levels were negatively correlated with triglyceride levels, a finding not commonly reported in other studies. This may indicate a novel aspect of thyroid hormone interaction with lipid metabolism, warranting further investigation. Our study's multiple linear regression analysis showed significant associations between waist circumference, fasting plasma glucose, and both TSH and FT4 levels, further supporting the interplay between thyroid status and metabolic syndrome components. These results are similar to those reported by Kalinowska *et al.*, who also found associations between FT4 and various metabolic parameters, including waist circumference and fasting plasma glucose [20].

Furthermore, the multivariate logistic regression analysis in our study identified systolic blood pressure and triglyceride levels as significant predictors of hypothyroidism in patients with metabolic syndrome. This finding is supported by the study conducted by Wu *et al.*, which also reported an increased risk of subclinical hypothyroidism associated with high blood pressure and high serum triglycerides [21]. The clinical implications of these findings suggest that patients with metabolic syndrome, particularly those with elevated blood pressure and triglyceride levels, should be closely monitored for thyroid dysfunction to mitigate the risk of cardiovascular complications.

CONCLUSION

The study concluded that the prevalence of hypothyroidism, both subclinical and overt, was notably high in individuals with metabolic syndrome, particularly among females, contributing to increased cardiovascular risk. Significant associations were found between TSH levels and several metabolic syndrome components, emphasizing the need for routine TSH monitoring in this population, especially in females. High systolic blood pressure and hypertriglyceridemia emerged as strong predictors of hypothyroidism in metabolic syndrome, underscoring their importance in patient management.

Recommendations

- Conducting a comprehensive large-scale study in which all limitations must be considered is necessary.
- All Mets patients need to be screened for hypothyroidism, and components of metabolic syndrome need to be searched in hypothyroid patients to reduce cardiovascular morbidity and mortality.

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