

Prevalence of Metabolic Syndrome among Adult Filipino Patients with Thyroid Disease in an Outpatient Clinic in Cebu City, Philippines from 2004–2015

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Abstract

Background: The Metabolic Syndrome (MetS) is a cluster of cardiovascular risk factors, which increases the risk for cardiovascular disease and stroke. In recent studies, thyroid disorder (TD) is associated with cardiovascular disease due to the effect of its hormones on the functions of the heart and should thus be considered an independent cardiovascular risk factor. The concurrence of MetS in persons with thyroid dysfunction may further increase their risk for cardiovascular events. In the Philippines, there is limited data regarding the prevalence of metabolic syndrome in patients with thyroid dysfunction, and at present no available local guidelines on the optimal time to screen patients with thyroid disorder for metabolic syndrome. We aimed to determine the prevalence of MetS and its components among adult Filipino patients with thyroid disorder.

Methods: This is a retrospective cross sectional study of 870 randomly selected patients previously diagnosed with thyroid disease in an outpatient clinic in Cebu City from year 2004 until 2015. Clinical data were obtained using an electronic medical search database. Anthropometric measures and BMI were recorded. Laboratory parameters including total cholesterol, triglycerides, HDL, LDL and fasting blood glucose were reviewed. Those patients who did not have any blood evaluations for metabolic parameters were excluded. Only 487 patients were included in the final analysis. Statistical analysis of the data was analyzed using the IBM SPSS Software version 21 and Chi square test of independence with 2x2 Fisher exact test adjustment wherein a p-value of <0.05 alpha was considered significant.

Findings: The overall prevalence of MetS in our patient population with diagnosed thyroid disease was 46%. MetS was noted in 54% of patients presenting with nontoxic goiter, 40% of patients presenting with thyrotoxicosis and only 6% in patients with hypothyroidism. The presence of MetS was more common among women (81%) with thyroid disorder than in men (19%), and more prevalent in the age group between 40 to 60 years of age. The components of MetS noted in our patient population were dyslipidemia (91%), diabetes (88%), obesity (75%) and hypertension (67%). There was no difference between genders with regard to the components of the MetS except the HDL and triglyceride levels.

Conclusion: In our study population, MetS was prevalent among patients presenting with thyroid disorder, especially in the female population above the age of 40. Screening for components of MetS is therefore advised on all patients seen in the outpatient setting for thyroid disorder. Our study has a valid clinical implication as undiagnosed components of metabolic syndrome will have poor long term prognosis in terms of morbidity and mortality. Early diagnosis and treatment of MetS, especially in patients with thyroid disorder who remain asymptomatic can result in better long term outcome.

Keywords: Metabolic syndrome; Thyroid disease; Dyslipidemia

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Introduction

Metabolic Syndrome (MetS) refers to a cluster of cardiovascular risk factors, whose underlying pathophysiology is thought to be related to Insulin Resistance (IR) [1-5]. The components include dyslipidemia, hypertension, raised triglycerides, abdominal obesity, and hyperglycemia [1-4]. These components increase the risk for cardiovascular disease and stroke.

The MetS is a known cardiovascular risk factor but its concurrence with thyroid dysfunction is not widely studied. There is paucity of data regarding the prevalence rate of MetS among patients with thyroid disease in general especially among euthyroid nontoxic goiters.

In 1988, Banting had described “a cluster of risk factors for diabetes and cardiovascular disease” and named it “Syndrome X”, which is now known as metabolic syndrome (MetS). The International Diabetes Federation (IDF) defines it as a cluster of cardiovascular risk factors, whose underlying pathophysiology is thought to be related to Insulin Resistance (IR) [6]. The components include dyslipidemia, hypertension, abdominal obesity and hyperglycemia [1, 7]. It is noted that people with MetS are twice as likely to die; and three times as likely to have a heart attack or stroke as with people without the syndrome [7]. People with MetS have a five-fold greater risk of developing type 2 diabetes and up to 80% of the 200 million people with diabetes globally will die of cardiovascular disease [7].

There are several clinical criteria used to define the MetS: National Cholesterol Education Program/Adult Treatment Panel (NCEP/ATP III) criteria, International Diabetes Federation (IDF) criteria and the NCEP/ATP III criteria modified by the American Heart Association/National Heart, Lung and Blood Institute (NCEP/ATP III-AHA/NHLBI) criteria. Each definition possesses common features; there are several parameters that differ, which results in difficulty in terms of applicability, uniformity, and positive predictive value with all these definitions [7]. Each has been described in previous reports.

Because of the differences in the criteria used by several epidemiologic studies, the prevalence of MetS varies greatly with locality and ethnicity [7]. The highest prevalence is found in the Middle East region, where more than every third person above the age of 20 fulfils the criteria for having the MetS [7]. In the National Health and Nutrition Examination Survey III (NHANES III) [7], the age-adjusted prevalence was 30–40 % higher in people of Mexican–American origin than in persons of White and African–American origin.

MetS incidence increases with age as the prevalence of obesity, hypertension, dyslipidemia and hyperglycemia also increases during this time [7]. Data regarding gender effect are conflicting with the majority of the studies [5] finding the highest prevalence in women, while the collaborative European analysis found no gender difference [7]. When applying the NCEP ATP III and the IDF criteria respectively to an Asian Indian population, the gender difference was higher using the NCEP-ATP III definition than when applying the IDF criteria [7-10].

In the Asia–Pacific Perspective [11] report for obesity in 2000, they note that increasing obesity was associated with increased risk for metabolic syndrome. In the report, they proposed that a lower BMI should be used among Asian population as there is an increased risk for cardiovascular disease with BMI>23 and higher in those with BMI of >25 [11]. Although most of the guidelines suggest the use of waist circumference (WC) as a measure of abdominal obesity, in a report by Geirach et al. [3], they noted that there is a significant correlation between BMI and WC. In our patient population, WC was not uniformly done and since all patients had a measured BMI, obesity in this study was based on BMI data and was included to define metabolic syndrome in the absence of the waist circumference. Geirach et al. [3] noted that the presence of overweight in men and even a normal body weight in women corresponds to an increase volume of visceral tissue in the abdomen.

In our locality, the prevalence of MetS was found to be 11.9% by NCEP/ATP III criteria, 14.5% by IDF criteria and 18.6% by NCEP/ATP III criteria modified by the American Heart Association/National Heart, Lung and Blood Institute (NCEP/ATP III-AHA/NHLBI) criteria. The most prevalent component was the low HDL-C [7, 10].

In most of these studies, the presence of MetS increased the risk for cardiovascular disease and stroke, as well as the tendency for myocardial infarction [7]. Many of the clinical criteria for MetS [7] however, did not include other identified risk factors for stroke (ie age, smoking), resulting in conflicting data.

Ogbera et al. [2] in 2012, reported on the association between cardiovascular disorders and thyroid disorders. As thyroid hormones affected the functions of the heart, Thyroid dysfunction (TD) was thought to be an independent cardiovascular risk factor. Ogbera et al. [2] reported that hypothyroidism was associated with the MetS; with females being more at risk than males. In 2009, by Shanta et al. [4] looked at euthyroid subjects and reported that free thyroxine (FT4) was found to be significantly related to some components of the MetS. Overt hypothyroidism has subsequently been recognized to be a risk factor for atherosclerotic cardiovascular disease, hyperlipidemia, low-grade inflammation and hypercoagulability [2]. Routine screening for cardiovascular risk factors in patients with thyroid disorders, especially in those with hypothyroidism has been recommended to unmask MetS [2].

The national prevalence of goiters in the Philippines was 3.7% in 1987 and increased to 6.7% in 1993 [7]. There has been no follow-up survey since then on goiter prevalence, nor has there been any national survey on the prevalence of thyroid dysfunction. In a survey done by the Philippine Thyroid Diseases Study (PhilTiDes) in 2008 on 4897 participants, it was found that 417 (8.53%) had thyroid function abnormalities, the most common abnormality being subclinical hyperthyroidism at a prevalence of 5.33% [3]. But no local study has been done to look at the prevalence of MetS among patients with thyroid disorder so that at present there are no available local guidelines on the optimal time to screen patients with thyroid disorder for metabolic syndrome.

In this study, we aim to determine the prevalence of the metabolic syndrome among adult Filipino patients with thyroid disorders and identify the risks contributing to the metabolic syndrome in such individuals.

Method

This is a retrospective cross sectional study of 870 randomly selected patients previously diagnosed with thyroid disease in a single physician outpatient clinic in Cebu City from year 2004 until 2015. Clinical data were obtained using an electronic medical search database.

The study included all patients who were more than 17 years old, all patients diagnosed with a goiter with or without an abnormal thyroid function test results and those with an abnormal thyroid function tests in the absence of goiter and all patients with a complete clinical history (particularly of thyroid disease, vital signs, height and weight) and laboratory data (total cholesterol, Triglycerides, HDL, LDL, FBS). All patients with history of thyroid malignancy or drug-induced hypothyroidism and all patients with liver disorders, renal disorders, congestive cardiac failure, pregnant women and patients on oral contraceptive pills were excluded from the study.

Data collection procedure

Prior to data collection, permission to access clinical case files from an outpatient clinic was obtained.

The patient census lists with a diagnosis of thyroid disease from the year 2004 to 2015 were reviewed at an outpatient clinic in Cebu City using an electronic medical data search. The following keywords were used: goiter, benign colloid nodule, multinodular goiter, Hashimoto's disease, Grave's disease, Plummer's disease, Autonomously Functioning Toxic Nodule (AFTN), hypothyroidism, and hyperthyroidism. Patients with incomplete clinical data and laboratory biochemical data were excluded from the study. Clinical data of each patient from the case files were reviewed recording the history pertaining to thyroid disease and presence of co-morbidities such as diabetes mellitus, hypertension and dyslipidemia.

The height and weight were documented and body mass index were calculated. The laboratory parameters such as fasting blood glucose, total cholesterol, high-density and low-density cholesterol and triglycerides were reviewed. The presence of MetS and its risk factors were identified.

Data processing

Patient with diagnosed thyroid disease were listed and retrospectively reviewed. The data were then encoded using Microsoft Office Excel 2007. Percentage distribution was used to describe the categorical data, the prevalence of metabolic syndrome and its components between gender and in thyroid disease.

Statistical analysis

To identify a significant difference between patients with thyroid disorder having metabolic syndrome and those without,

a Chi square test of independence with 2×2 Fisher exact test adjustment was performed wherein a p-value of <0.05 alpha was considered significant. The data was analyzed using the IBM SPSS Software version 21.0 program to ensure accuracy.

Results

Out of the 870 cases of thyroid dysfunction from the year 2014 to 2015, 383 cases were excluded based on exclusion criteria and those with incomplete clinical and laboratory data. Only 487 cases were included in the study for final analysis.

Metabolic syndrome was present in 46% (n=222) of the participants based on the NCEP/ATP III criteria and the inclusion of obesity as a component (**Figure 1**).

The clinical and laboratory characteristics of the subjects were reviewed in **Table 1** showing that majority of the subjects with thyroid disease were female (84%) with 43.8% already presented with metabolic syndrome. They were between the ages 40 to 60 years old (54.4%) and majority were classified as obese class I (41.5%). In the study, nontoxic goiter was the most common (50.5%), followed by thyrotoxicosis (43.1%) and hypothyroidism (6.4%).

Mets was seen predominantly among female (81%, $p=0.043$) and between the ages 40-60 years old ($p<0.01$). There was no significant difference in the type of thyroid disorder incidence in the subjects with MetS and those without (p -values >0.05 α).

Individual risk factors for MetS were determined. **Table 1** is showing that the most common component of MetS noted was dyslipidemia (91%, $p=0.014$), followed by diabetes mellitus (88%, $p<0.01$) and hypertension (67%, $p<0.01$). Triglyceride levels were significantly higher ($p<0.01$) while HDL levels were significantly lower ($p<0.01$) in the MetS group.

The clinical and laboratory characteristics of the subject population **Table 2** showed that majority of the patients with thyroid disorder were obese type 1 with a BMI of >25 . There was no significant difference noted ($p=0.479$) between genders. Triglyceride levels in male were significantly higher ($p=0.001$),

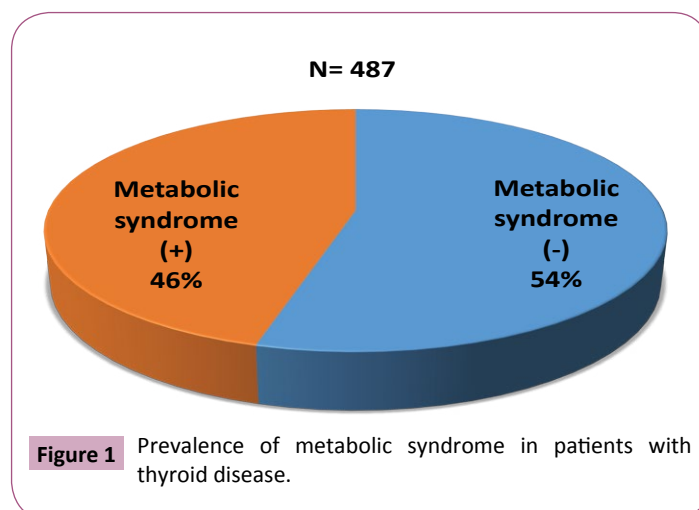


Table 1 Clinical and laboratory characteristics of subjects with and without metabolic syndrome.

Characteristics	Thyroid Disease		Metabolic syndrome (-)		Metabolic Syndrome (+)				p-value
	n=487		n=265		n=222				
					Females		Males		
Female	409	84%	230	87%	179	43.8%			0.043
Male	78	16%	35	13%			43	55.1%	
Age group									
<40 years old	153	31.4%	111	42%	32	20.9%	10	6.5%	<0.01
40-60 years old	265	54.4%	124	47%	113	42.6%	28	10.6%	
>60 years old	69	14.2%	30	11%	34	49.3%	5	7.3%	
Body Mass Index									
<18.5	9	1.8%	8	3%	1	11.1%	0	0%	<0.01
18.5-22.9	132	27.1%	106	40%	24	18.2%	3	2.27%	
23-24.9	85	17.5%	59	22%	23	27%	3	3.5%	
25-29.9	202	41.5%	71	27%	101	50%	30	14.9%	
≥ 30	59	12.1%	22	8%	30	50.1%	7	11.9%	
Goiter									
Thyrotoxicosis	210	43.1%	122	46%	67	31.9%	21	10%	0.126
Nontoxic Goiter	246	50.5%	127	48%	98	39.8%	21	8.5%	0.124
Hypothyroidism	31	6.4%	17	6%	13	41.9%	1	3.2%	0.556
Risk Factors									
Dyslipidemia	425	87.3%	222	84%	163	38.4%	40	9.4%	0.014
Total Cholesterol >200 mg/dl	235	48.2%	121	46%	95	40.4%	18	7.7%	0.491
LDL ≥ 100 mg/dl	342	70.2%	190	72%	126	36.8%	26	7.6%	0.224
Triglyceride ≥ 150 mg/dl	144	29.6%	23	9%	88	61.1%	33	22.9%	<0.01
HDL<40 mg/dl in Men	26	5.3%	5	2%	0	0%	22	84.6%	0.001
HDL<50 mg/dl in women	186	38.2%	57	22%	128	68.8%	0	0%	<0.01
Uncontrolled Diabetes	293	60.2%	97	37%	158	53.9%	38	12.9%	<0.01
FBS 100-125	184	37.8%	61	23%	97	52.7%	26	14%	<0.01
FBS>126 or DM	109	22.4%	36	14%	61	55.9%	12	11%	<0.01
BP ≥ 130/85 or hypertensive	194	39.8%	44	17%	125	64.43%	25	12.9%	<0.01

and low HDL was more common in the females ($p < 0.001$). Other clinical and laboratory characteristics were similar in both groups.

Based on the NCEP/ATP III criteria (**Table 3**) that included obesity as a measure, the population with MetS had at least 3 components present. In the population without MetS, 40% had 1 component and 40% had 2 components. Sub-analysis of the components showed that there was no significant difference between genders, p values ≥ 0.05 α (**Table 4**).

Among the known risk factors for MetS, dyslipidemia with a high LDL level was the most common component in patients with hypothyroidism, nontoxic goiter and thyrotoxicosis (**Table 5**), although the difference was not significant among the three groups with p value of >0.05 α . However, there was a significant difference in the presence of hypertension ($p=0.011$) in the nontoxic goiter population when compared to the other groups.

Discussion

MetS is a constellation of cardiometabolic factors with an incidence that has been progressively increasing worldwide [1]. These components increase the risk for cardiovascular disease and stroke [1, 2]. The concurrence of MetS in those with thyroid dysfunction may further increase the cardiovascular risk in such

individuals [2]. In this study, we determined the prevalence of MetS among Filipino patients with thyroid diseases seen in the outpatient setting.

In our study population, out of a total of 487 adult Filipino patients with thyroid disease reviewed, the prevalence of MetS using the NCEP/ATP III was noted to be 46%. Ogbera et al. [2] reported that about a fourth of their subjects from Nigeria with thyroid disorder had MetS with an overall prevalence of the MetS of 28%. In the same study, the frequency of metabolic syndrome in subjects with thyrotoxicosis, hypothyroidism and nontoxic goiter was 24%, 40% and 42%, respectively. The frequency of metabolic syndrome in our patient population for nontoxic goiter, thyrotoxicosis and hypothyroidism was 50.5%, 43.1% and 6.4%, respectively.

The major components of MetS in our study population were prevalent with the majority of patients presenting with dyslipidemia ($n=203$, $p=0.014$), diabetes mellitus (196, $p \leq 0.01$) and hypertension. There was a gender predisposition to women in terms of metabolic syndrome wherein 43.8% of the total study population has metabolic syndrome, and among those with MetS, 81% were women.

Dyslipidemia is often noted in thyroid dysfunction. Thyroid

Table 2 Clinical and laboratory characteristics of subjects with metabolic syndrome stratified by gender.

Characteristics	Total		Females		Males		p-value
	n=222		n=179		n=43		
Gender			179	81%	43	19%	0.043
Age group							
<40 years old	42	20%	32	18%	10	23%	0.911
40-60 years old	141	63%	113	63%	28	65%	
>60 years old	39	18%	34	19%	5	12%	
Body Mass Index							
<18.5	1	0%	1	1%	0	0%	0.479
18.5-22.9	27	12%	24	13%	3	7%	
23-24.9	26	12%	23	13%	3	7%	
25-29.9	131	59%	101	56%	30	70%	
≥ 30	37	17%	30	17%	7	16%	
Goiter							
Thyrotoxicosis	88	40%	67	38%	21	49%	0.130
Nontoxic Goiter	119	54%	98	55%	21	49%	0.298
Hypothyroidism	14	6%	13	7%	1	2%	0.205
Risk Factors							
Dyslipidemia	203	91%	163	91%	40	93%	0.525
Total Cholesterol>200 mg/dl	113	50%	95	53%	18	42%	0.112
LDL ≥ 100 mg/dl	152	68%	126	70%	26	60%	0.126
Triglyceride ≥ 150 mg/dl	121	54%	88	49%	33	77%	0.001
HDL<40 mg/dl in Men	21	9%	0	0%	22	51%	<0.001
HDL<50 mg/dl in women	129	58%	128	72%	0	0%	<0.001
FBS 100-125	123	55%	97	54%	26	60%	0.263
FBS>126 or DM	73	33%	61	34%	12	28%	0.280
BP ≥ 130/85 or hypertensive	150	67%	125	70%	25	58%	0.088

Table 3 Percentage of the components of metabolic syndrome.

Components	Total		Metabolic syndrome (-)		Metabolic syndrome (+)		p-value
	n=487		n=265		n=222		
0	52	10.6%	52	20%	0	0%	<0.01
1	107	22%	107	40%	0	0%	<0.01
2	106	21.8%	106	40%	0	0%	<0.01
3	122	25.1%	0	0%	122	54%	<0.01
4	80	16.4%	0	0%	80	35%	<0.01
5	20	4.1%	0	0%	20	9%	<0.01

Table 4 Distribution of the components of metabolic syndrome stratified by gender.

Components	Total		Females		Males		p-value
	n=487		n=409		n=78		
0	51	10.5	49	12%	2	3%	0.040
1	107	22	92	22%	15	19%	0.664
2	106	21.8	88	22%	18	23%	0.005
3	122	25.1	99	24%	23	29%	0.437
4	80	16.4	65	16%	15	19%	0.281
5	20	4.1	15	4%	5	6%	0.407

hormones influence LDL-C by various mechanisms including catabolism of LDL-C independent alterations in metabolism, stimulation of the synthesis of cholesterol as well as the influence on biliary lipid metabolism [2]. Reports [2-4] often show hypercholesterolemia and elevated LDL levels and low to normal HDL levels. In one study on patients with thyroid disorder [2], the mean levels of TG, TC and LDL-C were higher in persons with hypothyroidism than in other categories of TD, and statistically significant differences in the lipid parameters, TG and

LDL-C, were noted between subjects with hypothyroidism and other subjects with TD. In our study population, LDL levels were elevated in more than half of the patients with TD, but there was no significant difference noted among the different thyroid disorders ($p>0.05$ α). Among the subjects with MetS, there was a significantly higher TG value and lower HDL levels ($p<0.001$). There was no gender bias with regard to Total Cholesterol and HDL level between gender groups but triglyceride values were noted to be higher in men.

Table 5 Distribution of components of metabolic syndrome stratified by thyroid disorder.

Risk Factors	Hypothyroidism		Nontoxic Goiter		Thyrotoxicosis		p-value
	n=31		n=246		n=210		
Dyslipidemia	27	87%	223	91%	175	84%	0.065
Total Cholesterol>200 mg/dl	15	48%	121	49%	99	47%	0.889
LDL \geq 100 mg/dl	23	74%	184	75%	135	64%	0.051
Triglyceride \geq 150 mg/dl	11	35%	73	30%	60	29%	0.651
HDL<40 mg/dl in Men	0	0%	12	5%	14	7%	0.287
HDL<50 mg/dl in women	14	45%	100	41%	72	34%	0.286
FBS 100-125	8	26%	103	42%	73	35%	0.451
FBS>126 or DM	9	29%	50	20%	50	24%	0.453
BP \geq 130/85 or hypertensive	9	29%	114	46%	71	34%	0.011

Thyrotoxicosis is a significant cause of cardiac mortality and morbidity and systemic hypertension is a comorbidity that is found in half of the subjects with thyrotoxicosis [2]. The estimated prevalence rate of hypertension in thyrotoxicosis is around 37%.² This agrees with our data where the prevalence rate of hypertension in thyrotoxicosis was 34%. Hypertension was however also noted in 46% of patients with nontoxic goiters and 29% of patients with diagnosed hypothyroidism.

More significant in our study population is the large number of patients with thyroid disorder presenting with obesity based on initial BMI evaluation. The overall prevalence of obesity in our study population with thyroid disorder was 53.6%. The prevalence of obesity class I and II in men was 70% and 16% respectively, while in women it was 56% and 17% respectively.

Obesity is believed to predispose individuals to MetS through the development of insulin resistance [2-13] that in turn increases his risk for DM, hypertension and dyslipidemia. Over time, the presence of these components leads to MetS as seen in our study where most of the patients with thyroid disease over 40 years old had MetS. Among those without MetS, almost half of the subjects with thyroid disease already had at least 1 of the components. Failure to recognize these components early will increase the risk for developing MetS and in time increase their risk for cardiovascular disease.

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