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Metabolic syndrome and atherosclerotic cardiovascular disease risk assessment among adult patients with thyroid diseases in chemchemal chronic disease control-center, Sulaimania

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Abstract

Background and objectives: Metabolic syndrome is risk factor for atherosclerotic cardiovascular disease. The study's objective was to find the prevalence of metabolic syndrome among adult patients with thyroid diseases in Chemchemal chronic disease control center-Sulaimani, and to assess their atherosclerotic cardiovascular disease risk.

Methods: A cross-sectional analytical study conducted on 141 patients that attended the center; from 1st July 2018 to 1st January 2019. A structured questionnaire was administered and data was collected on socio-demographic, medical and behavioral history. Anthropometric measures and blood pressure were taken. Fasting venous blood samples were analyzed to measure lipids, glucose and thyroid hormones. The American Heart Association / National Heart, Lung, and Blood Institute criteria, was used for the definition of metabolic syndrome. Pooled Cohort Equation from the American College of Cardiology/ American Heart Association was used for atherosclerotic cardiovascular disease risk assessment of each patient.

Results: The prevalence of metabolic syndrome among thyroid patients was 80%, 78.7 % of females and 77.4% of males had metabolic syndrome. Hypothyroidism, central obesity and hypertension were significantly higher among females. Hypothyroidism was the major thyroid disease, found in 69.5% of the patients and thyrotoxicosis found in 30.5% of them. Atherosclerotic cardiovascular disease risk was high in majority of thyroid patients.

Conclusions: The prevalence of metabolic syndrome and atherosclerotic cardiovascular disease risk were significantly higher among thyroid patients than normal population.

Key words: Metabolic syndrome; Thyroid disease; Atherosclerotic cardiovascular disease risk.

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Introduction

Metabolic syndrome (MetS) is the coexistence of a group of risk factors that increases a person's probability for the development of type2 diabetes mellitus (DM) and cardiovascular disease (CVD). However the obesity is the main driving force behind it in most patients, those who are of normal weight may also be insulin resistant and may have the MetS[1].The thyroid diseases (TD), predominantly affects females and are common, occurring in about 5% of the population[2]. MetS risk factors increase the relative risk of developing CVD by twofold and diabetes by fivefold[3]. The American Endocrine Society recommends a 3-year screening interval for the MetS components in those with one or more. Calculation of the 10-year Atherosclerotic Cardiovascular Disease (ASCVD) risk is recommended in persons with MetS. The Pooled Cohort Equation (PCE) from the American College of Cardiology/ American Heart Association (ACC/AHA, 2013) is frequently used to determine the need for lifestyle modifications and therapeutic interventions, to prevent or delay progression to type2 DM or CVD[4]. In general populations the prevalence was as followings; in USA it was 28% for men 30% for women[1]. In India it was 11% in rural areas (ranged from 8.5%-25.8%) and 30% in urban areas (ranged from 16.7% to 41.7%) [5-7].In Iran it was 29% (37% for women and 29% for men) [8]. In Erbil, Iraq, it was 30.6% (45.5% for female and 16.3% for males) [9].Both MetS and hypothyroidism are independent risk factors for CVD and their coexistence increases this risk, with a considerable overlap in the pathogenic mechanisms of ASCVD [10-11]. Evidence suggests that MetS is associated with thyroid dysfunction and this affects MetS parameters[12-13]. Low normal free T4 levels and increased insulin resistance significantly associated, especially with hyperlipidemia. Hypothyroidism is well known cause of hyperlipidemia, diastolic hypertension, endothelial dysfunction, hypercoagulable state and CVD. These findings are consistent with an increased CVD risk in subjects with low normal thyroid function [14-16]. The Rotterdam Study concluded that subclinical hypothyroidism is a strong indicator of ASCVD in elderly women[16].A study found that, the hyperthyroid group had significantly lower level of total cholesterol (TC) and HDL-C, but a higher level of systolic BP, while abdominal obesity and

low HDL-C level, were more prevalent in the hyperthyroid group than the euthyroid group[17].MetS is one of the postulated mechanisms that clarify the association between TD and ASCVD, but the exact mechanisms are not clear yet [18].As thyroid hormones normally increases cardiac contractility and enhances cardiac output so increases BP in thyrotoxicosis; therefore it is a common comorbidity in thyrotoxic patients. In hypothyroidism there is a tendency to increase DBP as a result of increased systemic vascular resistance[19-21]. The objective of this study was to find the prevalence of MetS and its components among adult TP and assess their ASCVD risk, using (PCE), as no data is available about them in our region. This could be of value in highlighting the role of modifiable risk factors for developing of both MetS & ASCVD and contributes in the investments on programs of chronic diseases control and in the prevention and control of CVD.

Material and methods

A cross-sectional analytical study conducted on all thyroid patients that attended the chronic disease control center for regular monthly treatments in Chamchamal, Sulaimani governorate (on daily bases), from 1st July 2018 to 1st January 2019, starting from the approval of the research protocol by scientific and ethics committees at the Kurdistan Board of Medical Specialties(KBMS). During this period 141 adult thyroid patients, aged ≥18 years old, diagnosed previously by specialists attended the center. All included and assessed for MetS components and ASCVD risk.A structured questionnaire was administered. Data collected on socio-demographic, medical and behavioral history, gender, anthropometric measures [weight, height, Body Mass Index (BMI) and waist circumference (WC)], serum levels of fasting triglyceride (FTG), high density lipoprotein cholesterol (HDL), blood pressure (BP), and fasting blood glucose (FBG). Patient's total cholesterol (TC) was measured to evaluate their ASCVD risk. According to the American Heart Association / National Heart, Lung, and Blood Institute (AHA/NHLBI) qualifying measurements for the diagosis of MetS ,the patient must meet at least 3 of the 5 following criteria: WC ≥ 94 cm [37 in] in men or ≥ 80 cm [31.5 in] in women ; FTG) ≥150 mg/dl (1.7mmol/L) or drug therapy targeting increased triglyceride levels; fasting HDL levels less than < 40 mg/dl(1.0 mmol/L) in men and < 50 mg/dl (1.3

mmol/L) in women or drug therapy targeting decreased HDL cholesterol; systolic blood pressure (SBP) ≥130 mm Hg or diastolic blood pressure (DBP) ≥85 mm Hg or drug therapy for hypertension; and FBG ≥ 100 mg/dl (5.6 mmol/L) or drug therapy for increased glucose[4]. The data analyzed with Excel 2007 then with Statistical Package for the Social Sciences (SPSS version 22.0) and Social Science Statistics software. Each MetS component among different gender and thyroid status was compared. Group differences between the numbers of subjects were analyzed using Chi-squared test and p values ≤ 0.05 were considered statistically significant. Atherosclerotic Cardiovascular Disease (ASCVD) risk of each TP was estimated by (PCE).

Results

Overall 141 patients were on treatment of TD, the majority of them were females (78%, n=110), (80.9%, n=89) of them already presented with MetS and (22%, n=31)of the patients were males of these male patients, (77.4%, n=24) had MetS, so the prevalence of thyroid diseases is significantly higher among females(p = 0.037).The prevalence of MetS among all TP was (80.1%, n=113).The age of patients were ranging between 18 -88 years, the mean age was 51 years. Regarding the age groups: (20.6%, n=29) were aged from 18 to 39 years (young age group), (47.5%, n=67) were from 40 to 59 years (middle age group) and (31.9%, n=45) were aged ≥ 60 years (old age group).Hypothyroidism was the major thyroid disease, found in (69.5%, n=98) of all patients, (82.6%, n=81) were female and (17.4%, n=17) were males. Thyrotoxicosis found in (30.5%, n=43) of the patients, (67.4 %, n=29) of them were females, (32.6%, n=14) were males, Table (1).

Table (1): General characteristics of the patients.

Characteristics	Total n=141		MetS (-) n=28 (19.9%)			MetS(+) n=113 (80.1%)				
Gender	No	%	Female	Male	Total	Female		Male		Total
Women	110	78	21 75%		21 75%	89	78.7%			89 78.7%
Men	31	22		7 25%	7 25%			24	21.3%	24 21.3%
Age group										
18-39 years	29	20.6	11 52.4%	3 42.8%	14 50%	10	34.5%	5	20.8%	15 13.3%
40-59 years	67	47.5	6 28.6%	2 28.6%	8 28.6%	47	52.8%	12	50.0%	59 52.2%
≥60 years	45	31.9	4 19.0%	2 28.6%	6 21.4%	32	36.0%	7	29.1%	39 34.5%
Body Mass Index(BMI)										
<18.5 Underweight	1	0.7	0 0.0%	0 0.0%	0 0.0%	0	0.0%	1	4.16%	1 0.9%
18.5-24.9 Normal	8	5.6	2 9.5%	2 2 8.6%	4 14.2%	3	3.3%	1	4.2%	4 3.5%
↑BMI ≥25	132	93.6	19 90.5%	5 7 1.4%	24 85.7%	86	96.6%	22	91.7%	108 95.6%
25-29.9 Overweight	47	33.3	8 38.1%	3 42.8%	11 39.3%	23	25.8%	13	54.2%	36 31.8%
30-34.9 -Obesity class I	42	29.8	8 38.1%	2 2 8.6%	10 35.7%	27	30.3%	5	20.8%	32 28.3%
35-39.9 Obesity class II	25	17.7	3 14.3%	0 0.0%	3 10.7%	20	22.4%	2	8.3%	22 19.4%
≥40 Obesity class III	18	12.8	0 0.0%	0 0.0%	0 0%	16	18.0%	2	8.3%	18 15.9%
Thyroid State										
Thyrotoxicosis	43	30.5	8 38.1%	4 57.1%	12 42.9%	21	23.6%	10	42.0%	31 27.4%
Hypothyroidism	98	69.5	13 61.9%	3 42.9%	16 57.1%	68	76.4%	14	58.3%	82 72.6%

Among individual risk factors for MetS in all thyroid patients, central obesity (↑WC) was the most common component (89.4%, n=126), followed by ↑BP and hypertension (84.4%, n=119), then ↓HDL (81.5%, n=115) and ↑FBG (45.4%, n=64) followed by ↑FTG (44.7%, n=63), Table (2).

Table (2): Clinical and laboratory characteristics of the patients.

Characteristics	Total n=141		MetS (-) n=28 (19.9%)			MetS(+) n=113 (80.1%)				
Gender	No	%	Female n=21	Male n=7	Total n=28	Female n=89		Male n=24		Total n=113
MetS Components										
↑WC	126	89.4	18 85.7%	3 42.9%	21 75%	89	100%	16	66.6%	105 92.9%
Men WC ≥94	19	13.5	0 0.0%	3 42.9%	3 10.7%	0	0.0%	16	66.6%	16 14.2%
Women WC ≥80	107	75.8	18 85.7%	0 0.0%	18 64.3%	89	100%	0	0.0%	89 78.7%
FTG ≥ 150 mg/dl or on treatment hypertriglyceridemia	63	44.7	3 14.3%	1 14.3%	4 14.3%	44	49.4%	15	62.5%	59 52.2%
↓HDL	115	81.5	8 38.1%	3 42.9%	11 39.3%	85	95.5%	19	79.1%	104 92.0%
HDL<40 mg/dl in Men	22	15.6	0 0.0%	3 42.9%	3 10.7%	0	0.0%	19	79.1%	19 16.8%
HDL<50 mg/dl in women	93	65.9	8 38.1%	0 0.0%	8 28.6%	85	95.5%	0	0.0%	85 75.2%
FBG ≥100 or on treatment of DM	64	45.4	1 4.8%	1 14.3%	2 7.1%	51	57.3%	11	45.8%	62 54.8%
BP ≥130/85 mmHg or hypertensive	119	84.4	8 38.1%	3 42.9%	11 39.3%	85	95.5%	23	95.8%	108 82.4%

Regarding the prevalence of MetS no significant statistical difference between genders found (p =0.667), also for components, except for central obesity (↑WC) that was more common among females than males (p value <0.001) Table (3).

Table (3): Distribution of the components of the metabolic syndrome and thyroid status by gender.

Characteristics	**Total n=141**		**Female n=110**	**Male** n= 31	**p-value**
Total ↑WC	126	89.4%	107(97.3)	19(61.3%)	< 0.001
FTG ≥ 150 mg/dl or on treatment of hypertriglyceridemia	63	44.7%	47(42.7%)	16(51.6%)	0.379
Total ↓HDL	115	81.5%	93(84.5%)	22(71.0%)	0.851
FBG ≥100 or on treatment of DM	64	45.4%	52(47.3%)	12(38.7%)	0.397
FBG ≥126 or on treatment of DM	43	30.5%	35(31.8%)	8(25.8%)	0.520
SBP ≥130 or DBP≥85 mmHg or on hypertensive	119	84.4%	93(84.5%)	26(83.8%)	0.927
Hypertensive	98	69.5%	81(73.6%)	17(54.8)	0.044
Hypothyroidism	98	69.5%	81(73.6%)	17(54.8%)	0.044
Thyrotoxicosis	43	30.5%	29(26.3%)	14(45.2%)	0.044
Metabolic Syndrome	113	80.1%	89(80.9%)	24(77.4%)	0.667

Hypertension (BP ≥140/90 mmHg) was significantly higher among females (p = 0.044). Hypothyroidism was also significantly higher among females than males (p = 0.044), while thyrotoxicosis was significantly higher in males (p = 0.044).Regarding the distribution of components of MetS between hypothyroidism and thyrotoxicosis; no significant difference found between them, except (↓HDL) in female, which was more prevalent among hypothyroid females than thyrotoxic females, (p value < 0.03). Hypertension (BP≥140/90) was also significantly higher among TP than thyrotoxic patients. (p value = 0.019), Table(4).

Table (4): Distribution of the components of the metabolic syndrome by thyroid status and gender.

Characteristics	**Total** (n=141)		**Hypothyroidism** (n=98)		**Thyrotoxicosis** (n=43)		**p-value**
	Subtotal	%	Female n= 81	Male n=17	Female n=29	Male n=14	
Men WC ≥94	19	13.5%	0(0.0%)	9(52.9%)	0(0.0%)	10(71.4%)	0.292
Women WC ≥80	107	75.8%	78(96.3%)	0(0.0%)	29(100%)	0(0.0%)	0.949
Total ↑ WC	126	89.4%	78(96.3%)	9(52.9%)	29(100%)	10(71.4%)	0.733
FTG ≥ 150 mg/dl or on treatment hypertriglyceridemia	63	44.7%	36(44.4%)	10(58.8%)	11(37.9%)	6(42.6%)	0.415
HDL<40 mg/dl in Men	22	15.6%	0(0.0%)	12(70.6%)	0(0.0%)	10(71.4%)	0.959
HDL<50 mg/dl in women	93	65.9%	72(88.9%)	0(0.0%)	21(72.4%)	0(0.0%)	0.035
Total ↓HDL	115	81.5%	72(88.9%)	12(70.6%)	21(72.4%)	10(71.4%)	0.079
FBG ≥100 or on treatment of DM	64	45.4%	39(48.1%)	7(41.2%)	13(44.8%)	5(35.7%)	0.577
FBG ≥126 or on treatment of DM	43	30.5%	26(32.1%)	6(35.3%)	9(31.0%)	2(14.3%)	0.401
SBP ≥130 or DBP≥85 mmHg or on hypertensive	119	84.4%	69(85.2%)	15(88.2%)	24(82.8%)	11(78.6%)	0.515
Hypertensive	98	69.5%	61(75.3%)	13(76.5%)	20(60.0%)	4(28.6%)	0.019
Metabolic Syndrome	113	80.1%	68(83.9%)	14(82.4%)	21(72.4%)	10(71.4%)	0.112

As PCE estimates only Lifetime risk(LTR) for those patients aged from 20-39 years and LTR &10 year risk (TYR) for those aged from 40-59 years and only 10 year risk(TYR) for those aged from 60-79 years. The patients were classified to these age groups accordingly. Among the total of 141, two patients were younger than 20 years and another two were older than 79 years; these 4 patients (3 Females &1 Male) were excluded from ASCVD risk estimation. The remaining 137 patients were 107 females and 30 males. From these 137 patients, only 94 patients included in LTR estimation and 110 patients included in TYR estimation .In the youngest age group (20-39 years) which included 27 patients, most of them (63%, n=17) had a high LTR of ≥30%, (22.2%, n=6) had a

moderate LTR of 15-<30% and the remaining (14.8%, n=4) had a low LTR of <15%.The middle age group (40-59 years) included 67 patients, vast majority of them (92.5 %, n=62) had a high LTR ≥30 %,(4.5%, n=3) of them had a moderate LTR of 15-<30% and the remaining (3%, n=2) had a low LTR of <15%. The TYR among the same age group, showed that majority of them (80.6%, n=54) had a low TYR of <7.5 %,(13.4 %, n=9) had a moderate TYR of 7. 5-<20%, and the remaining (6.0 %, n=4) had a high TYR of ≥20%. In the oldest age group (60-79 years), that included 43 patients, most of them (60.5 %, n=26) had a high TYR of ≥20%, another (32.5 %, n=14) had a moderate TYR of 7.5-<20% and the remaining 7% (n=3) had a low TYR of <7.5%, Tables (5 and 6).

Table (5): Lifetime Risk (LTR) among thyroid patients.

ASCVDR				**Lifetime Risk(LTR)**								
Categories	Thyroid Patients			Low Risk (<15%)			Moderate Risk (15-<30%)			High Risk (≥30%)		
Age groups	T	F	M	T	F	M	T	F	M	T	F	M
20-39 years	27 28.7 %	19 26.4 %	8 36.4 %	4 14.8 %	4 21.0	0 0.0 %	6 22.2 %	6 31.6 %	0 0.0 %	17 63.0 %	9 47.4. %	8 100 %
40-59 years	67 71.3 %	53 73.6 %	14 63.6 %	2 3.0 %	1 1.9 %	1 7.1 %	3 4.5 %	3 5.7%	0 0.0 %	62 92.5 %	49 92.4 %	13 92.8 %
Total	94 100 %	72 100 %	22 100 %	6 6.4 %	5 6.9 %	1 4.5 %	9 9.6 %	9 12.5 %	0 0.0 %	79 84.0 %	58 80.6 %	21 95.5 %

T=Total, F=Female, M=Male

Table (6):10 Year Risk (TYR) among thyroid patients.

ASCVDR				**10 Year Risk(TYR)**								
Categories	Thyroid Patients			Low Risk (<7.5%)			Moderate Risk (7.5-<20%)			High Risk (≥20%)		
Age groups	T	F	M	T	F	M	T	F	M	T	F	M
40-59 years	67 60.9%	53 60.2%	14 63.6%	54 80.6%	45 84.9%	9 64.3%	9 13.4%	5 9.4%	4 28.6%	4 6.0%	3 5.7%	1 7.1%
60-79 years	43 39.1%	35 39.8%	8 36.4%	3 7.0%	3 8.6%	0 0.0%	14 32.5%	14 40.0%	0 0.0%	26 60.5%	18 51.4%	8 100%
Total	110 100%	88 100%	22 100%	57 51.8%	48 54.5%	9 40.9%	23 20.9%	19 21.6%	4 18.2%	30 27.3%	21 23.9%	9 40.9%

T=Total, F=Female, M=Male

Discussion

The Prevalence of MetS varies around the world, as they have different ethnicities and different diagnostic criteria applied, but generally stated that its prevalence increases with age, sedentary lifestyle and modernization[1].In this study, all TP attending the center in an outpatient setting, during the study period, were included and reviewed for components of MetS, according to the AHA/NHLBI criteria. The overall number was 141 patients. Female: Male ratio was about 4:1, similar to results of Hamlaoui (4:1), Ogbera (6:1) and Yu (4:1)[17-19].There was a gender predisposition of women to thyroid diseases, as females constitute 78% of the total TP and TD was significantly more prevalent in females (p = 0.037). In this study; thyroid male and female patients had significantly higher rates of MetS (77% and 81% respectively) than in Iraqi, Indian, Iranian and American men and women populations (p value <0.001)[1,5-9]. The prevalence of MetS was higher among females, but statistically not significant (p = 0.667), a similar finding to Hamlaoui (p=0.409) and Yu (p=0.065) studies[17, 19].The overall prevalence of MetS among TP was (80.1%, n=113), which was significantly higher than in general population (p < 0.001) [1, 5-9], also it's higher than that found by Hamlaoui (48.8%), Ogbera (28%) and Yu (46%) in TP, where Yu used the National

Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP III) criteria and Hamlaoui used modified NCEP/ATP III criteria and Ogbera used harmonized International Diabetes Federation (IDF) criteria [17-19]. In our study, hypothyroidism was more common than thyrotoxicosis (69.5% vs. 30.5%), which was similar to Hamlaoui study, but differed from Ogbera and Yu studies [17-19].The prevalence of MetS in hypothyroids was higher (83.7%) than in thyrotoxics (72.1%), with no significant difference (p = 0.113).Similar results found by Ogbera (40% vs.24%), but Yu found the opposite (6% vs. 40%). Hypothyroidism was significantly higher among females (p = 0.044), while thyrotoxicosis was significantly higher among males (p=0.044), similar to Hamlaoui study [17].In Ogbera's study thyrotoxicosis was more prevalent in both genders[18].Central obesity was our first major component of MetS (89.4%, n=126), followed by increased BP (84.4%, n= 119); these were similar to that of Hamlaoui, but was differed from those of Ogbera and Yu where increased FBG (46%) and dyslipidemia (87%) were the majors respectively[17-19]. 93.6% of our patients were obese (BM ≥ I25), that was higher than Yu's finding (53.6%) [19].In this study; high WC was significantly higher among females (97.3%) than males (61.3%) (p = 0.044) and all the females with MetS had central obesity, which constitute (79%, n=89) of TP with MetS (n=113).Central obesity was prevalent in both hypothyroidism (89%) and thyrotoxicosis (91%) with no significant difference; Hamlaoui found that 84.6% of hypothyroid patients had central obesity and also common among thyrotoxic patients[17]. In this study, no significant difference found between thyroid states regarding MetS components, except ↓HDL in female was significantly more prevalent among hypothyroid females than thyrotoxic females, (p = 0.035), while in Ogbera's study increased TG was the only defining criterion that was significantly higher in hypothyroid patients[18]. In this study, the prevalence of true hypertension (BP ≥140/90 mmHg) was significantly higher in hypothyroid patients (75.5%, n=74) than thyrotoxic patients (55.8%, n=24) (p = 0.019).A similar finding by Hamlaoui (51% vs. 50%) and Ogbera (60% vs. 33%) was noted but Yu found the reverse (29 % vs. 34%), with no significance [17-19]. Among thyrotoxic patients, true hypertension was significantly higher in females than males (p = 0.012).So hypothyroidism is a very important but overlooked cause of hypertension and thyroxine therapy usually leads to a marked reduction in BP, especially in young age group[22]. These different results may be justified by differences in ethnicities,

races, sample sizes and age of participants as well as different diagnostic criteria applied e.g.: NCEP/ATP III criteria, AHA/NHLBI criteria or IDF criteria and others.As MetS is multiplex risk factors for ASCVD (which includes: coronary heart diseases (CHD), cerebrovascular diseases (CVD), peripheral artery diseases and aortic atherosclerotic disease) and it is higher among thyroid patients, on the other hand thyroid diseases, especially hypothyroidism, are associated with CVD, in this study, PCE AHA/ACC, 2013, was used to estimate thyroid patients ASCVD risk and found that it was high in majority of them .Compared to subjects with optimal risk factors, thyroid patients had very higher ASCVD risk %, i.e. both LTR & TYR. The middle age group (40 to 59 years) had a very significantly higher prevalence of LTR (92.5%, n=62) than young age group (18-39 years) ($p < 0.001$). Vast majority (93%, n=40) of the old age group (60-79 years) had significantly moderate to high TYR ($p < 0.001$), while most of the middle age group (80.6%, n=54) had significantly low TYR ($p < 0.001$). These findings were consistent with the fact that Cardiometabolic risk (i.e. MetS) and ASCVD risk increase with age[1].

Conclusion

The prevalence of metabolic syndrome is significantly higher among thyroid patients than normal population and the ASCVD risk is also high in these patients, so ASCVD risk assessment is essential in patients with thyroid diseases to determine the need for lifestyle modifications and therapeutic interventions, to prevent or delay progression to type2 DM or ASCVD.

Conflict of interests

The authors recorded no conflict of interests.

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