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Original Article

Biochemistry Section

Association of Anti-TPO Antibodies with Insulin Resistance in Patients of Hypothyroidism with Metabolic Syndrome: A Cross-sectional Study

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ABSTRACT

Introduction: Hypothyroidism and Metabolic Syndrome (MetS) are associated with insulin resistance. Exact reason for development of insulin resistance in hypothyroidism is still unclear.

Aim: To determine the association between Anti-Thyroid Peroxidase Antibodies (Anti-TPO Abs) and Thyroid Stimulating Hormone (TSH) with components of MetS, Fasting Insulin (FSI) and Homeostatic Model Assessment Index for Insulin Resistance (HOMA-IR).

Materials and Methods: Total 118 subjects of hypothyroidism were included in this cross-sectional study. The diagnosis of MetS was made based on National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. Independent association of components of MetS, FSI and HOMA-IR with TSH and anti-TPO Abs was analysed by multivariate linear regression analysis.

Results: MetS was more prevalent in subclinical hyperthyroidism (53.0%) compared to overt hypothyroidism (49.3%). Serum anti-TPO Abs level was significantly high in MetS group compared to non-MetS group in both overt (200.0±170.2 and 122.8±98.9, p=0.02*) and subclinical (184.9±142.9 and 114.5±90.9, p=0.04*) hyperthyroidism. Waist Circumference (WC), Fasting Plasma Glucose (FPG), FSI and HOMA-IR were independently associated with anti-TPO Abs in both overt and subclinical hypothyroidism. Anti-TPO was also increased significantly in linear trend along with increased in the number of MetS components in both overt and subclinical hypothyroidism.

Conclusion: MetS is highly prevalent in hypothyroidism and anti-TPO Abs rather than TSH and is more associated with insulin resistance in patients of hypothyroidism with MetS.

Keywords: Autoimmunity, Fasting plasma glucose and fasting insulin, Thyroid hormones

INTRODUCTION

Hypothyroidism is the most common endocrinal chaos with prevalence of around 10-11% in the population of urban India [1]. Thyroid hormones play a vital role in regulating energy homeostasis, glucose and lipid metabolism. Thyroid dysfunction has been associated with insulin resistance, dyslipidemia and Cardiovascular Diseases (CVD) [2,3]. Thyroid Peroxidase (TPO) plays a crucial part in thyroid hormone synthesis by oxidation of iodine and coupling of iodotyrosine in thyroglobulin. Presence of Anti-TPO Abs in autoimmune thyroid diseases inhibits TPO competitively, fixes the complement and destroys thyroid cells. Hence the presence of anti-TPO is a hallmark of autoimmune thyroid disease. Anti-TPO is highly prevalent in thyroid hypo function and excess level is significantly associated with rapid worsening of thyroid function [4]. Exact pathogenesis of occurrence of insulin resistance is still imprecise. Elevated levels of TSH in hypothyroidism may affect secretion of insulin and may be responsible for occurrence of insulin resistance and MetS [5]. Imbalance between anti and pro-inflammatory cytokines may be accountable for insulin resistance in hypothyroidism. It has also been suggested that cellular and molecular interaction other than thyroid hormones may be implicated in occurrence of insulin resistance [6].

MetS is a major health alarm all over the world. Prevalence of MetS is around 40.9% in the North Indian region and it is increasing rapidly, even in the age group of less than 40 years [7]. In MetS, presence of biochemical, physiological, clinical and metabolic abnormalities have been associated with increased risk for incidence of Type 2 Diabetes Mellitus (T2DM) and CVD. Advanced age, overweight, sedentary life, insulin resistance and hormonal imbalance are significant risk factors for occurrence of MetS [8]. Auto-immunity and systemic inflammation produced by adipokines from adipose tissue have been associated with development of MetS [9].

Autoimmunity [4,9] and systemic inflammation [6,9] may be associated with occurrence of insulin resistance [6,8] in hypothyroidism and MetS. Thyroid function and components of MetS are also influenced by genetic and geographical factors. Thyroid functions influence MetS components including plasma glucose, High Density Lipoprotein-Cholesterol (HDL-c), Triglycerides (TAG) and blood pressure [10,11]. It is relevant to estimate the occurrence of MetS in patients of hypothyroidism as both have few common pathogenesis and presence of both have been associated with high risk for occurrence of CVD compared to presence of any one [12]. Based on above background, the aim of the study was to estimate the occurrence of MetS in hypothyroidism patients and to determine association between Anti-TPO Abs and TSH with components of MetS, FSI and HOMA-IR.

MATERIALS AND METHODS

The hospital based cross-sectional study was carried out from October 2009 to December 2011, in the Department of Biochemistry of Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi, India. The study was approved (N.11/IEC/MAMC2009) by the ethical committee of Maulana Azad Medical College, New Delhi and conducted according to amendments of the 1964 Helsinki Declaration. Informed consent was acquired from all the study participants.

Inclusion criteria: Total 118 patients who attended the endocrine clinic during the study period and newly diagnosed cases of subclinical (defined as high TSH and normal serum level of fT_3 (Triiodothyronine) and fT_4 (Thyroxine)) or overt hypothyroidism

(defined as elevated TSH and decreased serum levels of T_4 or T_3) were included in the study [13] through convenient sampling.

Exclusion criteria: Subjects with known diabetes with or without treatment, liver, renal and heart failure, ascites or abdominal mass, women with polycystic ovarian syndrome, pregnant women, receiving any medication that may alter thyroid function and lipid profiles (like lithium, proton pump inhibitors, anticonvulsants, and steroids) were excluded from the study.

Diagnosis of MetS was performed by criteria of NCEP ATP III. Based on this criteria, the diagnosis of MetS was documented when three or more of the following components were identified: WC: >102 cm in men and >80 cm in women; TAG ≥ 150 mg/dL in either sex or on specific medicine of this dyslipidemia; HDL-C <50 mg/dL in women and <40 mg/dL in men or on specific medicine of this dyslipidemia, FPG ≥110 mg/dL and blood pressure: Systolic Blood Pressure (SBP) ≥130 mm Hg, Diastolic Blood Pressure (DBP) ≥85 mm Hg or on specific medicine of hypertension [14].

Study Protocol

The detailed history including demographic profile and clinical findings were documented in the prepared proforma. Blood pressure was measured by manual sphygmomanometer containing mercury column. Before measurement of blood pressure, participants were instructed to take rest for at least 5 minutes in seated position. By keeping manual sphygmomanometer at participant's heart level and, systolic and diastolic pressure was measured three times in the left arm. Minimum 5 minutes of gap was kept between the each measurement. Average of three readings was calculated and it was considered as the final recorded value of blood pressure. WC was measured by non-stretchable standard measuring tape in the horizontal plane at the superior border of iliac crest and the average of two measurements was considered as final measurement. Five mL of fasting blood was collected in plain vial and fluoride vial by venepuncture between 8-9 AM from all study participants. Serum TAG, HDL-C and FPG estimation was done by using commercial kits modified to random access Clinical Chemistry Analyser (Beckman Coulter DXC 800, USA). Fasting serum fT_3, fT_4, TSH, anti-TPO and insulin were estimated using Electrochemiluminescence based immunoassay (ECLIA) modified to Roche–Elecsys 2010 (Germany). If value of anti-TPO Abs was reported >34.0 IU/mL then it was considered as a positive [15]. HOMA-IR was calculated by using this formula: {FSI in mIU//L X FPG in mg/dL}/405 and HOMA-IR of >2.5 was considered as high insulin resistance [16]. First insulin resistance was calculated in 20 cases of hypothyroidism in pilot study. Six cases had HOMA-IR of >2.5. Hence, prevalence of high HOMA-IR was 30.0% in hypothyroidism patients. By using 30% prevalence, sample size was calculated by using this formula: Sample size=$(Z^2)\times(pq)\div L^2$ (Z=Confidence interval, p=prevalence, q=1-prevalance and L=absolute error of 10%). Based on this calculation, sample size was 84.

STATISTICAL ANALYSIS

Statistical analysis was performed on Statistical Package for the Social Sciences (SPSS) software version 17. Categorical variables were described in percentage and number continuous variables were described in mean and Standard Deviation (SD). Chi-square test was used to compare categorical variables and student's t-test and one-way Analysis of Variance (ANOVA) test were used to compare continuous variables. Univariate linear regression was used to find association of variables with anti-TPO Abs and TSH. Multivariate linear regression was used to find independent association of variables with anti-TPO Abs and TSH. A p-value of <0.05 was considered as significant.

RESULTS

The age range of study participants was between 25 and 77 years and the mean age was 46.8 years. Out of total 118 participants studied, 69 (58.5%) were in the overt hypothyroid group and 49 (41.5%) were in subclinical hypothyroid groups. Total, 60 (50.8%) individuals out of 118 cases of hypothyroidism had MetS. The prevalence of MetS was 49.3% in overt and 53.0% in subclinical hypothyroid groups. The occurrence of MetS was found to be non-significant in overt and subclinical hypothyroidism (p=0.68). Similarly male and female subjects were almost equal in both groups with more numbers of females (n=22 and n=16) in overt and subclinical hypothyroid groups, respectively [Table/Fig-1].

	Overt hypothyroid			Subclinical hypothyroid			Total	p-value
	Male	Female	Total	Male	Female	Total		
MetS	12 (17.4%)	22 (31.9%)	34 (49.3%)	10 (20.4)	16 (32.6)	26 (53.0)	60 (50.8%)	0.68^{NS}
Non-MetS	11 (15.9%)	24 (34.8%)	35 (50.7%)	9 (18.4)	14 (28.6)	23 (47.0)	58 (49.2%)	
Total	69 (58.5%)			49 (41.5%)			118 (100.0%)	

[Table/Fig-1]: Distribution of Metabolic Syndrome (MetS) in study participants. Chi-square test was used to calculate p-value. *p-value <0.05 significant, **p-value <0.001 ^{HS}: Highly significant, ^{NS}-Not significant

Serum fT_3 and fT_4 levels were comparable between MetS and non-MetS groups and it was found regardless of severity of hypothyroid state. Serum TSH level was significantly high in MetS group compared to non-MetS group in overt hyperthyroidism (14.6±4.3 and 11.5±3.6, p=0.002). Such a difference was not significant in subclinical hypothyroid group. Serum anti-TPO level was significantly high in MetS group compared to non-MetS group in both overt (200.0±170.2 and 122.8±98.9, p=0.02) and subclinical hyperthyroidism (184.9±142.9 and 114.5±90.9, p=0.04), as depicted in [Table/Fig-2].

[Table/Fig-3] depicts the mean and SD of MetS components, FSI and HOMA-IR in study participants. WC, SBP, DBP, FPG, and TAG were significantly higher in the MetS group compared to non-MetS group in both overt and subclinical hypothyroidism. FPG was significantly higher in MetS group of overt (121.8±19.2, p<0.001) and subclinical (125.0±33.1, p<0.001) hypothyroidism compared to non-MetS group. There was no significant difference of HDL in MetS and non-MetS groups in both overt and subclinical hypothyroidism. FSI was significantly higher in the MetS group compared to non-MetS group only in overt hyperthyroidism (25.7±11.8 and 16.9±8.5, p=0.02). HOMA-IR was significantly higher in Mets group compared to non-MetS group in both overt (6.1±2.8 and 3.1±1.2, p≤0.001) and subclinical hypothyroidism (4.9±1.9 and 2.2±1.0, p≤0.001).

[Table/Fig-4] depicts distribution of different variables according to different categories of Anti-TPO Abs and TSH level. MetS cases were significantly high in category of Anti-TPO Abs >34.0 IU/mL and TSH ≥10.0 mIU/L. WC, DBP, FPG, FSI and HOMA-IR were significantly high in category of Anti-TPO Abs >34.0 IU/mL and WC, DBP and FPG were significantly high in category of TSH ≥10.0 mIU/L. Anti-TPO Abs of >34.0 IU/mL were highly and significantly associated with HOMA-IR compared to anti-TPO Abs of ≤34.0 IU/mL (5.7±2.1 and 3.2±1.5, p <0.001). However, high TSH level of ≥10.0 mIU/L was not associated with HOMA IR compared to TSH level of <10.0 mIU/L (4.3±1.7 and 3.9±1.2, p=0.15).

[Table/Fig-5] depicts the association of variables with fT3, TSH and Anti-TPO Abs in multivariate linear regression. Age, gender and other components of MetS were adjusted during analysis. WC was independently negatively associated with fT3 in both overt and subclinical hypothyroidism. DBP was independently associated with TSH in both groups, while FPG and TAG were independently associated with TSH only in overt hyperthyroidism. WC (β=0.32, p=0.02 and β=0.30, p=0.03), FPG (β=0.32, p=0.03 and β=0.30, p=0.04), FSI (β=0.36, p=0.01 and β=0.31, p=0.01) and HOMA-IR (β=0.38, p=0.008 and β=0.34, p=0.009) were independently

	Overt hypothyroid				Subclinical hypothyroid			
	fT_3 (pmol/L)	fT_4 (pmol/L)	TSH (mIU/L)	Anti-TPO Abs (IU/mL)	fT_3 (pmol/L)	fT_4 (pmol/L)	TSH (mIU/L)	Anti-TPO Abs (IU/mL)
MetS	2.73±0.7	7.30±2.0	14.6±4.3	200.0±170.2	5.1±1.1	16.2±2.8	9.15±2.0	184.9±142.9
Non-MetS	2.40±0.7	6.60±1.5	11.5±3.6	122.8±98.9	5.6±1.3	15.0±2.4	8.24±2.1	114.5±90.9
p-value	0.07^{NS}	0.10^{NS}	0.002*	0.02*	0.15^{NS}	0.11^{NS}	0.15^{NS}	0.04*

[Table/Fig-2]: Mean and SD level of serum fT_3, fT_4, TSH and anti-TPO Abs in study participants.
Student's t-test was used to calculate p-value. *p-value <0.05 significant, **p-value <0.001 HS (highly significant), NS-Not significant

	Overt hypothyroid			Subclinical hypothyroid		
	MetS (Mean±SD)	Non-MetS (Mean±SD)	p-value	MetS (Mean±SD)	Non-MetS (Mean±SD)	p-value
WC (cm)	93.7±9.1	83.3±6.3	<0.001**^{HS}	94.2±8.1	84.5±6.1	<0.001**^{HS}
SBP (mm Hg)	136.7±17.1	127.6±12.7	0.01*	138.4±15.4	123.0±11.1	0.001**^{HS}
DBP (mm Hg)	89.2±9.7	83.9±7.1	0.01*	91.3±10.6	84.2±7.3	0.009*
FPG (mg/dL)	121.8±19.2	90.7±16.0	<0.001**^{HS}	125.0±33.1	89.2±10.2	<0.001** ^{HS}
TAG (mg/dL)	198.1±58.6	136.3±33.1	<0.001**^{HS}	175.2±52.0	155.3±45.6	0.16^{NS}
HDL-C (mg/dL)	41.9±8.3	44.2±8.2	0.25^{NS}	41.7±8.98	44.6±8.8	0.26^{NS}
FSI (uIU/L)	25.7±11.8	16.9±8.5	0.02*	17.8±7.9	14.5±6.2	0.11^{NS}
HOMA-IR	6.1±2.8	3.1±1.2	<0.001**^{HS}	4.9±1.9	2.2±1.0	<0.001**^{HS}

[Table/Fig-3]: Mean and SD level of components of Metabolic Syndrome (MetS) in overt and subclinical hypothyroidism.
WC: Waist circumference; SBP: Systolic blood pressure, DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; TAG: Triacylglycerol; HDL-C: High density lipoprotein-cholesterol; FSI: Fasting insulin, HOMA-IR: Homeostatic model assessment index for insulin resistance; Students t-test was used to calculate p-value. *p-value <0.05 significant, **p-value <0.001 ^{HS}: Highly significant, ^{NS}: Not significant

	Hypothyroidism					
	Anti-TPO Abs			TSH		
	≤34.0 IU/mL	>34.0 IU/mL	p-value	<10.0 mIU/L	≥10.0 mIU/L	p-value
No. of MetS (%)	17 (14.4)	43 (36.4)	0.003*	25 (21.2)	35 (29.7)	0.47^{NS}
No. of Non-MetS (%)	32 (27.2)	26 (22.0)		28 (23.7)	30 (25.4)	
Age (Years, Mean±SD)	48.9±11.4	47.9±12.3	0.65^{NS}	49.3±10.8	48.5±11.9	0.70^{NS}
WC (cm, Mean±SD)	88.9±9.23	95.5±10.7	0.001**^{HS}	89.5±9.79	94.3±8.92	0.006*
SBP (mm Hg, Mean±SD)	128.3±19.2	131.2±22.2	0.46^{NS}	126.3±18.4	129.5±23.4	0.41^{NS}
DBP (mm Hg, Mean±SD)	82.3±17.2	88.9±15.6	0.03*	84.2±13.5	90.1±14.7	0.02*
FPG (mg/dL, Mean±SD)	109.9±14.7	128.5±15.6	<0.001**^{HS}	115.7±12.4	122.8±19.2	0.02*
TAG (mg/dL, Mean±SD)	169.5±30.2	171.2±45.2	0.81^{NS}	179.4±23.5	188.9±58.9	0.27^{NS}
HDL-C (mg/dL, Mean±SD)	41.2±11.9	39.2±10.2	0.32^{NS}	43.9±12.4	40.2±10.2	0.07^{NS}
FSI (uIU/L, Mean±SD)	17.1±7.8	23.6±10.2	<0.001**^{HS}	16.9±6.9	17.3±5.8	0.70^{NS}
HOMA-IR (Mean±SD)	3.2±1.5	5.7±2.1	<0.001**^{HS}	3.9±1.9	4.3±1.7	0.15^{NS}

[Table/Fig-4]: Comparison of different variables according to anti-TPO Abs and TSH level in study participants.
Univariate linear regression was used to calculate p-value. *p-value <0.05 significant, **p-value <0.001 ^{HS}: Highly significant, ^{NS}: Not significant

	Overt hypothyroid						Subclinical hypothyroid					
	fT_3		TSH		Anti-TPO		fT_3		TSH		Anti-TPO	
	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value
WC	-0.33	0.03*	0.20	0.11	0.32	0.02*	-0.26	0.04	0.01*	0.99	0.30	0.03*
SBP	-0.08	0.95	0.13	0.29	0.17	0.25	-0.14	0.26	0.11	0.39	0.16	0.16
DBP	0.03	0.79	0.20	0.04*	0.11	0.30	0.06	0.64	0.29	0.02*	0.11	0.32
FPG	-0.17	0.17	0.29	0.01*	0.32	0.03*	0.02	0.85	0.19	0.18	0.30	0.04*
TAG	-0.17	0.18	0.23	0.03*	0.17	0.18	-0.02	0.86	0.20	0.05	0.13	0.22
HDL	-0.02	0.84	0.14	0.27	0.15	0.21	-0.19	0.14	0.04*	0.75	0.14	0.20
FSI	-0.20	0.19	0.22	0.08	0.36	0.01*	-0.29	0.06	0.21	0.07	0.31	0.01*
HOMA-IR	-0.26	0.21	0.25	0.06	0.38	0.008*	-0.31	0.08	0.24	0.09	0.34	0.009*

[Table/Fig-5]: Association of the MetS components with fT3, TSH and anti-TPO in study participants.
Multivariate linear regression was used to find association. *p-value <0.05 significant, **p-value <0.001 ^{HS}: Highly significant, ^{NS}-Not significant. β: Regression coefficient

associated with Anti-TPO Abs in both over and subclinical hypothyroidism. HOMA-IR was not independently associated with TSH in multivariate linear regression analysis.

Overall 20.6% cases in overt hypothyroidism and 15.5% cases in subclinical hypothyroidism had all five components of MetS. Anti-TPO Abs were increased in linear trend in the presence of more positive components of MetS in overt (p=0.04) and subclinical (p=0.03) hypothyroidism [Table/Fig-6].

DISCUSSION

In this study, the prevalence of MetS was 49.3% in overt and 53.0% in subclinical hypothyroid groups. This study shows that the prevalence of MetS is high in hypothyroid patients. Similarly, Erdogan M et al., have reported prevalence of 44% in overt and 35% in subclinical hypothyroidism [17]. Ogbera AO et al., have also reported prevalence of 40% in subclinical hypothyroidism [18]. So, it alleges that hypothyroid subjects are more prone for occurrence of MetS.

Number of MetS components	Overt hypothyroid			Subclinical hypothyroid		
	N (%)	Anti-TPO Abs (IU/mL)	TSH (mIU/L)	N (%)	Anti-TPO Abs (IU/mL)	TSH (mIU/L)
Three	17 (50.0)	90.0±61.5	12.2±3.1	15 (57.6)	80.2±75.3	8.2±2.1
Four	10 (29.4)	140.4±105.2	12.7±4.2	7 (26.9)	142.8±86.2	7.9±2.8
Five	07 (20.6)	207.2±170.1	13.2±5.3	4 (15.5)	187.0±65.2	8.5±3.4
p-value	-	0.04*	0.82^{NS}	-	0.03*	0.92^{NS}

[Table/Fig-6]: Frequency of components of Metabolic Syndrome (MetS) in study participants and their association with anti TPO Abs and TSH.
Univariate linear regression was used for analysis. *p-value <0.05 significant, **p-value <0.001 ^{HS}: Highly significant), ^{NS}: Not significant

In the present study, TSH level was found to be significantly high in subjects of MetS in overt hypothyroidism. Ruhula S et al., have also reported a significant association of high normal TSH with MetS [19]. Increase occurrence of MetS has also been found in euthyroid individuals even with high normal TSH level [20]. This disparity may be due to either: (a) commencement of MetS exacerbates the hypothyroid condition; or (b) risk of occurrence of MetS increases as severity of hypothyroidism increases. The second possibility is excluded because the disparity in TSH level between MetS and non-MetS groups was not statistically significant in subclinical hypothyroidism and the prevalence of MetS wasn't found to be statistically different in overt and subclinical hypothyroidism. Results of the study are in agreement with a large extent study reported by Park SB et al., [21], in which higher levels of TSH predict the occurrence and risk of MetS in overt hypothyroidism but not in subclinical hypothyroidism.

WC is one of the key components for reorganisation in MetS. In the present study, the WC was independently negatively associated with serum fT_3 level in both overt and subclinical hypothyroidism. Khatiwada S et al., have also observed similar finding [22]. Defective lipid metabolism and independently association of TAG with TSH in hypothyroidism might be the reason of high WC in these subjects. In this study, serum TAG was independently associated with TSH only in overt hypothyroidism, not in subclinical hypothyroidism. Serum TAG was not independently assosiated with serum fT_4 and fT_4. It suggests that TSH is a superior predictor of altered lipid metabolism compared to fT_4 and fT_4. The elevation of TAG in hypothyroidism is caused by a reduced removal rate of TAG from plasma due to a decrease in the activity of hepatic TAG lipase [23]. Hypothyroidism has been associated with decreased activity of TAG lipase in liver which results in diminish TAG's plasma removal rate and hypertriglyceridemia. TSH also impairs lipolysis by inhibiting adipose TAG lipase via protein kinase A pathway as reported by Jiang D et al., [24].

FPG was independently associated with serum TSH levels in subjects of MetS with overt hypothyroid group. Thyroid hormones interact with insulin and regulate its action via GLUT-4 in adipose tissue and skeletal muscle and also stimulate lipolysis [25]. This explains the independent association of serum TSH with FPG. However, FPG was not independently associated with TSH in subclinical hypothyroidism. Minor disturbance of TSH level in subclinical hypothyroidism might be a cause for failure of statistical significance. Derangements in metabolism of lipids depend on severity of hypothyroid as TAG was more elevated in overt hypothyroidism compared to subclinical hypothyroidism.

DBP was significantly associated with TSH level in both overt and subclinical hypothyroidism. Khatiwada S et al., have also observed similar association of DBP with TSH [22]. This association might be due to increased arterial stiffness and systemic vascular resistance in hypothyroidism [26]. It has been reported that thyroxine treatment in hypothyroidism may reduce arterial stiffness, vascular resistance, DBP and mean arterial pressure in both type of hypothyroidism [27].

In univariate analysis, anti-TPO Abs positive cases (>34.0 IU/mL) had a significant high level of WC, DBP, FPG, FSI and HOMA-IR compared to anti-TPO Abs negative cases in hypothyroidism. But only WC, FPG, FSI and HOMA-IR were independently associated with anti-TPO Abs in both overt and subclinical hypothyroidism, in multivariate linear regression analysis. Thus, HOMA-IR was independently associated with anti-TPO Abs in multivariate linear regression, but not with TSH. Anti-TPO was also increased significantly in linear trend along with increased in the number of MetS components in both overt and subclinical hypothyroidism. It suggests that Anti-TPO Abs rather than TSH is more accountable for occurrence of insulin resistance in patients of hypothyroidism with MetS as TSH is not positively associated with HOMA-IR in multivariate linear regression analysis. Chen Y et al., have reported positive association of thyroid autoimmunity with central obesity and HOMA-IR [28]. Mazaheri T et al., have also reported high prevalence of elevated FSI in presence of excess anti-TPO Abs compared to low titre of anti-TPO Abs (94.1% and 62.8%, p-value=0.05) [29].

Antibodies against TPO specific antigen produce an immune complex which activates complement pathway and T cells, resulting in surplus synthesis of pro-inflammatory cytokines like IL-6 and TNF-α [30]. Thus, the link between Anti-TPO Abs and proinflammatory cytokine may be responsible for development of insulin resistance in patients of hypothyroidism with MetS.

Limitation(s)

Only new cases of hypothyroidism were selected in the study as thyroxine treatment in old cases may affect the component of MetS. It was a hospital-based study and requires external validation.

CONCLUSION(S)

Hypothyroidism is associated with increased prevalence of MetS. Anti-TPO Abs rather than TSH is more associated with occurrence of insulin resistance in patients of hypothyroidism with MetS. Hypothyroidism patients should be screened for anti-TPO and MetS regardless of the severity of the hypothyroidism.

Population based study on large sample size with measurement of pro-inflammatory cytokines should be done for further validation of study results.

Contribution: Design and conception: AJ, SD, PL, LC, DD; Collection and gathering of data: AJ, SD, MM; Clinical monitoring and laboratory detection: AJ, SD, MM, PL; Data analysis and interpretation: AJ, SD, MM; Manuscript preparation: AJ, SD, MM; Approval of manuscript: All authors.

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