



Original Research Article

Prevalence of thyroid dysfunction in metabolic syndrome - A cross-sectional study

Shravya R Ginnaram¹, D Sridevi^{1,*}, Amrut Arvindrao Dambal¹, Sushritha Y Reddy¹, Abhinav R Pingle¹¹Dept. of Biochemistry, Malla Reddy Institute of Medical Sciences, Hyderabad, Telangana, India

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ABSTRACT

Background and Objectives: Literature review have hypothesized that the rising incidence of metabolic syndrome worldwide has been associated with an increased risk of thyroid disorders. The aim & objective of our study was to diagnose patients with metabolic syndrome based on IDF criteria, to estimate T3, T4, TSH levels among these patients and to observe the correlation between thyroid dysfunction and metabolic syndrome.

Materials and Methods: Our study was a hospital based age and sex matched cross-sectional study with a total of 120 participants (60 cases and 60 controls) between 30 - 50 years old conducted at Malla Reddy Institute of Medical Sciences, Hyderabad, India. Ethics approval was obtained from the Institutional Ethics Committee.

Results: Our study found that both men and women with metabolic syndrome had a higher percentage of thyroid disorders compared to the controls without metabolic syndrome. Among the cases, women were found to present with more thyroid abnormalities than men.

Conclusion: Routine screening with thyroid function tests should be implemented for all patients with metabolic syndrome, especially females. The coexistence of these two entities can increase the risk for cardiovascular disease. Early detection and intervention can help reduce the progression of CVD.

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1. Introduction

Metabolic Syndrome (MetS) is a constellation of risk factors that as a group have a greater predictive ability for disease than when considered separately, which may be indicative of future cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) in adults.¹

They include: central obesity, elevated triglycerides (TG), low high-density lipoprotein cholesterol (HDL-C), raised blood pressure (BP) and raised fasting blood glucose. The presence of three or more of these risk factors indicates MetS. It is also associated with pro-thrombotic and pro-inflammatory states.²

Insulin resistance is a central component of metabolic syndrome.³ Increasing body fat, especially visceral fat,

is also associated with an increase in the prevalence of metabolic syndrome.

The ongoing epidemic of obesity appears to have affected all sectors of the population over the past several years due to increased calorie consumption and sedentary lifestyles.^{4,5} Increasing rates of obesity are proportional to the increase in the prevalence of T2DM, CVD, high blood pressure, sleep apnea, and certain cancers.⁶

Thyroid hormones have a profound effect on energy homeostasis, fatty acid and glucose metabolism and blood pressure.⁷ Therefore, there is a probability that functional changes in the thyroid gland might have an association with MetS and its related components.⁸ Thyroid-stimulating hormone (TSH) directly correlates with insulin resistance, TG and indirectly with HDL-C.⁹

Hypothyroidism is characterized by elevated levels of TSH with decreased levels of T3 and T4.

* Corresponding author.

E-mail address: sridumedico@gmail.com (D. Sridevi).

Subclinical hypothyroidism (SCH), characterized by elevated TSH levels with normal levels of T3 and T4, is more common than overt hypothyroidism with a prevalence of 1.4–7.8% in asymptomatic older individuals and even greater percentiles among women.¹⁰

Hyperthyroidism is characterized by decreased levels of TSH with elevated levels of T3 and T4. Subclinical hyperthyroidism (SCH) is characterized by decreased levels of TSH with normal levels of T3 and T4.

The current study aims to investigate the prevalence of thyroid dysfunction in metabolic syndrome and to study the association between thyroid disorders and the components of metabolic syndrome.

2. Materials and Methods

This study was taken up in Malla Reddy Institute of Medical Sciences, Hyderabad, India. Ethical clearance was obtained from the Institutional ethics committee. This was a hospital based cross-sectional study with a total of 120 age and sex matched subjects (60 cases and 60 controls) between 30–50 years old were selected from the outpatient departments of General Medicine and Obstetrics and Gynecology. The study was conducted between May - August 2015. Detailed proper informed consent was taken from all the subjects.

2.1. Inclusion criteria (Based on IDF definition)

After proper physical and biochemical analysis of the subjects the following were the criteria for inclusion:

Central adiposity (Waist circumference \geq 90 cm in males and \geq 80 cm in females) plus two or more of the following four factors:

1. Serum Triglycerides: \geq 150mg/dl
2. Serum HDL cholesterol: <40 mg/dl in men and <50 mg/dl in women
3. Blood pressure: Systolic Blood Pressure \geq 130 mmHg or Diastolic Blood Pressure \geq 85 mmHg
4. Fasting plasma glucose concentration of \geq 100 mg/dl.

2.1.1. Cases

Subjects fulfilling the criteria for MetS were included as cases.

2.1.2. Controls

Apparently normal and healthy subjects without MetS were considered as controls.

2.2. Exclusion criteria

1. Subjects under treatment for thyroid disorders, dyslipidemia.
2. Patients on drugs which alters glucose and thyroid hormone metabolism like steroids, antipsychotics
3. Pregnancy.

4. Significant hepatic, renal or cardiovascular disease.

2.3. Anthropometry

Waist circumference was measured at the midpoint between the lower margin of the lowest palpable rib and the top of the iliac crest, at the end of a normal expiration using a non-stretchable fiber measure tape, with the tape held parallel to the floor.

After a period of 15 minutes rest, blood pressure (BP) was measured as SBP and DBP in the right upper limb with the help of a sphygmomanometer in the supine position, placing the sphygmomanometer at the level of the heart.

2.4. Biochemical tests

Fasting morning blood samples (5ml) were collected by anterior cubital vein venipuncture in a plain red top vacutainer for separation of serum. The sample was set aside for 15 minutes to clot. The specimens were centrifuged to separate the serum and analyzed. Fasting glucose was determined by the GOD-POD method.

Serum cholesterol was detected by the enzymatic CHOD/POD method. Serum HDL-C was estimated by direct method.¹¹ Serum triglyceride was estimated by Glycerol Phosphate Oxidase/Peroxidase (GPO/POD) colorimetric endpoint method. LDL-C was obtained using Friedwald's formula as given below:

$LDL-C = \text{Total cholesterol} - (\text{HDL-C} + \text{VLDL-C})$.¹² TSH, Total T3 and Total T4: were estimated by Chemiluminescence immunoassay (CLIA) using neolumax.

2.5. Statistical methods

Data was analyzed by applying appropriate statistical tests by using SPSS package version number 20.

Data was expressed in terms of mean \pm SD. Student's 't' test was applied to estimate the difference between the two groups of the population. P value < 0.05 was taken as significant.

3. Results

A hospital based cross-sectional study was carried out to study the prevalence of thyroid dysfunction among males and females with and without metabolic syndrome

Mean WC in male controls was 87.17 ± 1.82 compared to cases with 103.13 ± 6.46 displaying a highly significant statistical difference ($p < 0.0001$). Mean WC in female controls was 78.23 ± 4.39 compared to cases with 94.07 ± 8.22 displaying highly significant statistical difference ($p < 0.0001$) (Tables 1 and 2).

Mean SBP in male controls was 121.20 ± 7.92 compared to cases with 127.80 ± 10.91 displaying a significant statistical difference ($p=0.0095$). Mean SBP in female controls was 114.60 ± 9.88 compared to cases with

123.93 ± 15.80 displaying a significant statistical difference ($p=0.0081$). (Tables 1 and 2).

Mean DBP in male controls was 78.73 ± 6.40 compared to cases with 84.0 ± 8.98 displaying a significant statistical difference ($p =0.0011$). Mean DBP in female controls was 74.07 ± 8.62 compared to cases with 81.20 ± 9.54 displaying a significant statistical difference ($p =0.0036$). (Tables 1 and 2).

Mean FPG in male controls was 95.23 ± 12.71 compared to cases with 113.03 ± 18.61 displaying a highly significant statistical difference ($p <0.0001$). Mean FPG in female controls was 92.90 ± 8.66 compared to cases with 107.67 ± 14.89 displaying a highly significant statistical difference ($p <0.0001$). (Tables 1 and 2).

Mean TG in male controls was 126.50 ± 49.10 compared to cases with 180.97 ± 91.18 displaying a significant statistical difference ($p =0.0056$). Mean TG in female controls was 103.03 ± 28.83 compared to cases with 158.23 ± 86.85 displaying a significant statistical difference ($p =0.0016$). (Tables 1 and 2).

Mean HDL in male controls was 40.60 ± 6.01 compared to cases with 37.07 ± 4.18 displaying a significant statistical difference ($p = 0.0106$). Mean HDL-C in female controls was 47.73 ± 8.16 compared to cases with 41.30 ± 6.83 displaying a significant statistical difference ($p = 0.0016$). (Tables 1 and 2).

Mean T3 in male controls was 1.09 ± 0.25 compared to cases with 1.02 ± 0.28 and is not significant ($p = 0.3542$). Mean T3 in female controls was 1.51 ± 1.78 compared to cases with 1.06 ± 0.27 and is not significant ($p = 0.1739$). (Tables 1 and 2).

Mean T4 in male controls was 9.12 ± 1.93 compared to cases with 8.82 ± 2.54 and is not significant ($p =0.6104$). Mean T4 in female controls was 9.61 ± 1.53 compared to cases with 9.51 ± 2.05 and is not significant ($p =0.8218$). (Tables 1 and 2).

Mean TSH in male controls was 2.18 ± 1.21 compared to cases with 3.89 ± 3.75 displaying a significant statistical difference ($p =0.0209$). Mean TSH in female controls was 2.76 ± 1.52 compared to cases with 6.44 ± 9.14 displaying a significant statistical difference ($p =0.0339$). (Tables 1 and 2).

4. Discussion

In this study, we found that 16.7% among male metabolic syndrome patients (overt hypothyroidism 3.3% and subclinical hypothyroidism 13.33%) and 30% among female metabolic syndrome patients (overt hypothyroidism 6.66% and subclinical hypothyroidism 23.33%) exhibited thyroid dysfunction. In the control group, 3.33% males and 6.66% females had subclinical hypothyroidism. In a recent population-based study among the adult population in India, the prevalence of hypothyroidism was 3.9% while that of subclinical hypothyroidism was 9.4%.¹³

According to the report by Shantha et al., the prevalence of overt hypothyroidism was 7.4% and that of subclinical hypothyroidism was 21.9% in the MetS population.¹⁴

In this study, the prevalence of thyroid dysfunction was more in females compared to males, comparable to the study by Uzunlulu et al.¹⁵ Therefore, we recommend the routine screening of thyroid function in patients with MetS, particularly among females.

This study showed a significant association of thyroid dysfunction with MetS in both males and females ($P = 0.004$). A significant difference was found in the mean values for each anthropometric and biochemical parameters among patients with MetS and healthy control subjects; only T3 and T4 were not significantly altered. Thus, thyroid dysfunction was found to be related to all the components of MetS. These findings were similar to those obtained by Kota et al., who mentioned body mass index (BMI), WC, mean systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood glucose (FBG), total cholesterol, low density lipoprotein cholesterol (LDL-C), TG, and TSH were significantly higher in the MetS group compared to the control group and HDL-C was significantly lower in the study group.¹⁶ Similar findings were found in the study conducted by Meher et al.¹⁷

We found no correlation between TSH and all the components of MetS in our study. The study by Wang et al.¹⁸ showed no statistical correlation between subclinical thyroid disease and MetS, in contrast to the significant correlation reported in the study by Kim et al.¹⁹ In this study, we did not find any case of hyperthyroidism in contrast to the work done by Jayakumar.²⁰

Both systolic and diastolic blood pressure were found to be significantly increased in subclinical hypothyroid women. TSH levels were found to have a positive correlation with blood pressure. In a large population study, a positive linear association was established between systolic and diastolic arterial pressure and TSH levels.²¹ Reduced thyroid function can increase peripheral vascular resistance and activate the sympatho-adrenal system, increasing the BP, particularly DBP.²²

Insulin resistance is the key pathologic factor for the progression of metabolic syndrome and is the cardinal promotive factor for T2DM, dyslipidemia and thyroid dysfunction proven by the study conducted by Singh BM et al, who concluded that there was a significant correlation between TSH and insulin.²³ Bakker et al. demonstrated interactions between insulin resistance and thyroid function in euthyroid non diabetic adults. Their observations stated that insulin resistance increases the deleterious effect of hypothyroidism on lipid profile reflecting the association of insulin resistance with low serum HDL-C and increased TGs.²⁴

Serum levels of TSH are a reliable index of the biological activity of thyroid hormones. Some studies

Table 1: Comparative study of male cases with controls

Males Parameters	Controls		Cases		P Value	Significance
	MEAN	SD±	MEAN	SD±		
WC(cm)	87.17	1.82	103.13	6.46	*<0.0001	Highly Significant
SBP(mm of Hg)	121.20	7.92	127.80	10.91	*0.0095	Significant
DBP(mm of Hg)	78.73	6.40	84.0	8.98	*0.0113	Significant
FBS(mg/dl)	95.23	12.71	113.03	18.61	*<0.0001	Highly Significant
TG(mg/dl)	126.50	49.10	180.97	91.18	*0.0056	Significant
HDL(mg/dl)	40.60	6.01	37.07	4.18	*0.0106	Significant
T3(ng/ml)	1.09	0.25	1.02	0.28	0.3542	Not Significant
T4 (µg/dl)	9.12	1.93	8.82	2.55	0.6104	Not Significant
TSH (mIU/L)	2.18	1.21	3.89	3.75	*0.0209	Significant

*p<0.05 is significant

Table 2: Showing comparative study of female cases with controls

Females Parameters	Controls		Cases		P Value	Significance
	MEAN	SD±	MEAN	SD±		
WC(cm)	78.23	4.39	94.07	8.22	*< 0.0001	Highly Significant
SBP(mm of Hg)	114.60	9.88	123.93	15.80	*0.0081	Significant
DBP(mm of Hg)	74.07	8.62	81.20	9.54	*0.0036	Significant
FBS(mg/dl)	92.90	8.66	107.67	14.89	*< 0.0001	Highly Significant
TG(mg/dl)	103.03	28.83	158.23	86.85	*0.0016	Significant
HDL(mg/dl)	47.73	8.16	41.30	6.83	*0.0016	Significant
T3(ng/ml)	1.51	1.78	1.06	0.27	0.1739	Not Significant
T4 (µg/dl)	9.61	1.53	9.51	2.05	0.8218	Not Significant
TSH (mIU/L)	2.76	1.52	6.44	9.14	*0.0339	Significant

P <0.05 is significant

Table 3: Prevalence of thyroid dysfunction in males

	Cases	Controls	Total
Thyroid dysfunction	5	1	6
Euthyroid	25	29	54
Total	30	30	60

Table 4: Prevalence of thyroid dysfunction in females

	Cases	Controls	Total
Thyroid dysfunction	9	2	11
Euthyroid	21	28	49
Total	30	30	60

Table 5: Prevalence of thyroid dysfunction in males and females combined

	Cases	Controls	Total
Thyroid dysfunction	14	3	17
Euthyroid	46	57	103
Total	60	60	120

showed that adipocytes and preadipocytes expressed TSH receptors to which TSH would bind and induce preadipocytes to produce and release adipokines like leptin playing an important role in the onset of metabolic syndrome and cardiovascular disease.²⁵ Leptin regulates TRH expression²⁶ and insulin increases the total Leptin levels.²⁷ Thus, increased abdominal fat along with insulin resistance may contribute to increased serum TSH levels via serum leptin concentrations.²⁸

In conclusion, the prevalence of thyroid dysfunction, distinctively Subclinical Hypothyroidism in patients with MetS was found to be high with females being at an increased risk. Although thyroid hormones significantly affect each component of MetS, there was no relationship found between thyroid dysfunction and all of the components of MetS. There is an increased incidence of thyroid dysfunction, especially elevated TSH with normal T4 and T3 in MetS. Furthermore, the coexistence of the two disease entities might substantially increase the risk of Arterio Sclerotic Cardio Vascular Disease (ASCVD), hence it is worthwhile to order TSH and FT4 levels in all patients with MetS.

5. Source of Funding

ICMR.

6. Conflict(s) of Interest

Nil

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Author biography

Shravya R Ginnaram Student

D Sridevi Associate Professor

Amrut Arvindrao Dambal Professor

Sushritha Y Reddy Student

Abhinav R Pingle Student

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