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Subclinical Thyroid Dysfunction In Subjects With Metabolic Syndrome

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Abstract:
Context: *Metabolic Syndrome (MetSyn) is a clustering of interrelated cardiovascular risk factors. Subclinical hypothyroidism (SCH) is known to be a risk factor for adverse cardiovascular outcomes. The association between SCH and MetSyn has been found to be inconsistent.*
Aims: *To determine the prevalence of SCH amongst subjects with MetSyn, and to study the association of serum TSH with components of MetSyn.*
Settings and Design: *Thirty subjects with MetSyn and thirty healthy subjects were enrolled as cases and controls, respectively.*
Methods and Materials: *Fasting blood sugar (FBS), serum triglycerides, serum total cholesterol, serum low density lipoprotein (LDL), serum high density lipoprotein (HDL), serum thyroid stimulating hormone (TSH), serum free thyroxine (fT4) and serum free triiodothyronine (fT3) were studied.*
Statistical Analyses Used: *Student's "t" test, Fishers exact test and Pearson correlation coefficient were used.*
Results: *The proportion of SCH in subjects with MetSyn was 23.3%. Waist circumference, mean systolic pressure, diastolic pressure, FBS, total cholesterol, LDL, triglycerides and TSH were significantly higher in the cases, and HDL ($p< 0.001$), and fT3 ($p = 0.014$) were significantly lower, as compared to the controls. A significant association between SCH and MetSyn ($p = 0.02$) was observed. TSH showed positive linear association with waist circumference, triglycerides, LDL, and negative association with HDL, in the cases.*
Conclusions: *A significant relationship between SCH and MetSyn, and between serum TSH levels and some components of Metabolic Syndrome exists, but more comprehensive studies, with larger sample sizes, are needed to establish the relationship between SCH and MetSyn.*
Keywords: *Subclinical hypothyroid dysfunction, metabolic syndrome, Thyroid stimulating hormone*

I. Introduction

Subclinical hypothyroidism, an isolated elevation of thyroid stimulating hormone (TSH) levels with a normal free thyroxine (fT4) levels, is a relatively common disorder amongst otherwise healthy, young, middle-aged and older adults. [1], [2] Individuals with subclinical hypothyroidism are usually asymptomatic, but may manifest with cardiac dysfunction, adverse cardiac end points (atherosclerotic disease and cardiovascular mortality), elevated low-density lipoprotein, neuropsychiatric symptoms, and may progress to overt, symptomatic hypothyroidism. Treatment may impede progression to overt hypothyroidism, reduce symptoms, improve cardiac contractility, correct abnormal serum lipids, decrease goiter size, and reduce risk of adverse fetal effects in postpartum hypothyroidism. [1], [2]The prevalence of subclinical hypothyroidism in a study conducted in Delhi was 19.3% (15.9% men, 21.4% women), and that of subclinical hyperthyroidism was 1.13%. This prevalence is rapidly rising in Indian subjects and it is estimated that about 42 million Indians suffer from thyroid disease, both subclinical and overt. [3]

Metabolic Syndrome is the clustering of interrelated modifiable cardiovascular risk factors that includes central adiposity, hypertension, hyperglycemia, high triglycerides with low high density lipoprotein cholesterol levels, tendency to form blood clots, insulin resistance and inflammation. Metabolic syndrome is known to strongly predict the long-term risk of diabetes mellitus and atherosclerotic cardiovascular disease. [4] The associations and clustering of these factors have been known for decades. The increasing prevalence of metabolic syndrome can be attributed to changes in nutrition, lifestyle and socioeconomic status, rural-to-urban migration, increasing obesity and sedentary lifestyles.[4] Prevalence of metabolic syndrome in an Indian population is 33.5% (24.9% in males, 43.2% in females), according to a study conducted in urban Orissa on 1178 subjects and 22.3% (25% in males and 22% in females) in an adult population in rural Karnataka.[5], [6] Numerous definitions have been proposed for metabolic syndrome.[7], [8], [9], [10]

According to the updated present AHA/NHLBI statement (Modified NCEP ATPIII criteria) the presence of any three of the following five modifiable cardiovascular risk factors would make a clinical diagnosis of metabolic syndrome. [11], [12], [13]

1. Elevated waist circumference (WC) (with ethnicity specific values for South Asians) ≥90 cm in men and ≥80 cm in women,
2. Elevated serum triglycerides ≥150 mg/dL or
3. Reduced serum high density lipoprotein cholesterol(HDL) <40 mg/dL in men and <50 mg/dL in women
4. Elevated blood pressure ≥130 mm Hg systolic blood pressure and/or ≥85 mm Hg diastolic blood pressure or on antihypertensive drug treatment in a patient with a history of hypertension,
5. Elevated fasting glucose (FBS) ≥100 mg/dL or on drug treatment for elevated glucose.

However, studies exploring the association between Serum TSH and components of metabolic syndrome in subjects with subclinical thyroid dysfunction are few and with differing conclusions. [14], [15], [16] Therefore, the aim of the present study was to investigate the proportion of subjects having subclinical thyroid dysfunction amongst the metabolic syndrome population and the association of TSH with the components of metabolic syndrome.

II. Materials And Methods

A case controlled study was conducted at M S Ramaiah Medical College & Hospitals, Bangalore, after required approval from the Institutional Ethical Committee (Ref No. ECR/215/Inst/Ker/2013). The duration of the study was 3 months (February 2014 to May 2014) and the sample size was 60 (30 Cases and 30 Controls). The scientific basis for sample size was as follows-based on a study conducted by Chugh K et al., on Thyroid Function Tests in Metabolic Syndrome, it was found that TSH (mIU/mL) values as expressed in terms of mean and standard deviation in patients with Metabolic Syndrome was 5.68 +/- 1.90 and in normal individuals was 2.19 +/- 0.94.So, with confidence level of 95% and with power of 95%, the required sample size for the present study was estimated to be 60 (30 cases and 30 controls). [17] Subjects aged between 18-50 years who came to the diagnostic laboratory for a routine health checkup and who fulfilled three out of the five criteria for a diagnosis of metabolic syndrome according to the updated present AHA/NHLBI statement (Modified NCEP ATP III criteria- as detailed above) were included as cases. The healthy individuals who did not have any criteria for a diagnosis of metabolic syndrome were selected as controls. Subjects who had a history of thyroid dysfunction (hyper or hypothyroidism) or on treatment with thyroxine and antithyroid drugs, pregnant women or those who were within first year of post partum period, patients on any medication that may affect thyroid function - Corticosteroids, Lithium, anti-thyroid drugs, p-aminosalisylic acid, interferon-alpha & other cytokines, Amiodarone, Cyanates, Tyrosine Kinase inhibitors or Iodine^{131} treatment, patients with acute illnesses, autoimmune diseases, connective tissue diseases, myocardial infarction, malignancy, familial hyperlipidaemia, chronic liver and kidney diseases and post-menopausal women were excluded from the study. Demographic, socioeconomic and self reported behavioural information (smoking, alcohol, physical activity and diet), objective measures of anthropometry (height, weight, waist and hip circumferences) were collected from all study participants. After a written and informed consent was taken, about 3mL of blood was collected, with due aseptic precautions after an overnight fast (no calorific intake) of 8-12 hours, from each study subject, in the phlebotomy section of the diagnostic laboratory. The blood samples were allowed to clot and were centrifuged at 4000 rpm for 8-10 minutes. After separation, the following lab investigations were done on the samples on Roche Cobas 6000 c501, fully automated analyzer at the diagnostic laboratory-Fasting blood sugar (FBS) by Hexokinase method, Serum total cholesterol (TC)by enzymatic colorimetric method using cholesterol oxidase, Serum triglyceride (TG) by enzymatic colorimetric method using glycerol phosphate oxidase, Serum high density lipoprotein cholesterol (HDL)- enzymatic colorimetric method using cholesterol oxidase and esterase, Low density lipoprotein cholesterol (LDL) estimated by direct Assay based on precipitation method. All of the assays were routinely monitored by participation in external quality-control programs and using assayed chemistry and assayed immunoassay plus controls (Bio-Rad Lab, Hercules, CA, USA).

After the above investigations, the serum samples were stored at -20 °C in the diagnostic laboratory and Serum TSH, fT4, and free triiodothyronine (fT3) measurements were made by using colorimetric enzyme-linked immunosorbent assay (Calbiotech Inc., 10461 Austin Dr, Spring Valley, CA, USA). The analytical sensitivity of TSH was 0.005 µIU/mL, for fT4 was 0.005 ng/dL, and for fT3 was 0.05 pg/mL. Normal range for TSH was 0.4 to 4.2 µIU/mL, for fT4 was 0.8 to 2.0 ng/dL, and for fT3 was 1.4 to 4.2 pg/mL. Subjects were considered as euthyroid when they had normal TSH, fT4 and fT3 levels. Subclinical hypothyroidism was defined as a TSH concentration of 4.20-10.0 µIU/mL with a normal fT4 and fT3 concentration.[18]

III. Statistical Analysis

Baseline characteristics of the study participants were expressed in mean ± SD and percentage. Student's "t" test was used to analyze differences in baseline characteristics between the study group and the control group. Fisher's exact test was used to analyze the association between Metabolic Syndrome and subclinical hypothyroidism. Pearson correlation was used to determine if any significant relationship between the components of metabolic syndrome and TSH levels existed. p value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS windows version 17.0 software (SPSS Inc., Chicago, IL, USA).

IV. Results

There were 30 subjects in the metabolic syndrome group, of which 17(56.6%) were males and 13(43.33%) were females. Amongst the 30 healthy subjects included as controls in the study, the number of males was 16(53.33%) and number of females was 14(46.66%). In the metabolic Syndrome group, 7 (23.3%- 5 females and 2 males) subjects had subclinical hypothyroidism and 23(76.66%) were euthyroid. Amongst the healthy controls, all 30 (100%) subjects were euthyroid. Subclinical hypothyroidism had significant association with Metabolic Syndrome when assessed by two tailed Fisher's exact test, with $p = 0.0105$. Clinical and biochemical characteristics of the study groups are given in Table 1. The two groups were similar with respect to age and gender distribution. Waist circumference (WC), mean systolic pressure (SBP), diastolic pressure (DBP), fasting blood sugar, total cholesterol, LDL, triglycerides, and TSH were significantly higher in the Metabolic Syndrome group compared to the control group. HDL and fT3 were significantly lower in cases [Table 1]. The relationship of TSH and fT4 levels with the presence of components of Metabolic Syndrome was assessed using Pearson correlation coefficient analysis and is shown in Table 2 and Table 3. There was a statistically significant positive correlation between TSH (μIU/ml) and Waist Circumference ($r = 0.491$, $p < 0.001$), Serum Triglyceride($r = 0.874$, $p <0.001$) and Serum LDL ($r= 0.885$, $p<0.0001$) and a statistically significant negative correlation between TSH and serum HDL ($r = -0.711$, $p<0.001$) in the metabolic syndrome group. In healthy controls, there was a statistically significant positive correlation between TSH with Waist Circumference ($r = +0.446$, $p= 0.013$) and Serum LDL ($r=0.5303$, $p=0.002$) and a statistically significant negative correlation between TSH and Serum HDL($r = -0.385$, $p= 0.036$). In metabolic syndrome subjects, serum fT4 was negatively associated with waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood sugar and HDL. It was positively associated with serum triglycerides and Serum LDL. But none of these associations were statistically significant except the positive correlation with Serum LDL($r=0.408$, $p=0.02$). In healthy controls, serum fT4 was negatively associated with waist circumference, systolic blood pressure, diastolic blood pressure, serum LDL and serum triglycerides. It was positively associated with fasting blood sugar and HDL. The association between fT4 with waist circumference ($p=0.003$) and HDL ($p=0.049$) was statistically significant in the healthy controls.

V. Discussion

This cross-sectional study was undertaken, in order to determine the proportion of metabolic syndrome subjects having subclinical hypothyroid dysfunction and to determine the association between serum TSH and various components of metabolic syndrome, in the diagnostic laboratory of M S Ramaiah Medical College and Hospitals, Bangalore. The Metabolic Syndrome group included 30subjects with 17 males and 13 females, while the control group included 30 subjects with 16 males and 14 females. The two groups were similar in their distribution of age ($p = 0.345$) and gender.

The proportion of subclinical thyroid dysfunction in subjects with metabolic syndrome was 23.3% in the present study. This finding is in agreement with previous studies showing an association between Metabolic syndrome and thyroid dysfunction. A study by Gyawali et al. in Nepal showed a prevalence of subclinical hypothyroidism of 29.32% in the metabolic syndrome group.[19] A study done in Behrampur, Orissa by Meher et al. showed a prevalence of subclinical hypothyroidism of 22% and overt hypothyroidism of 4% in the Metabolic Syndrome group.[20] The prevalence of subclinical hypothyroidism was 21.90% and that of overt hypothyroidism 7.4%, in patients with Metabolic Syndrome as found by Shantha et al. in Chennai, South India.[21] In a study by Wang et al., in a Taiwanese population, 4.55% had subclinical hypothyroidism and 2.64% had subclinical hyperthyroidism. [15] Another study by Uzunlulu et al. in Turkey showed 16.4% subjects of metabolic syndrome to have subclinical hypothyroidism.[16] The present study did not find any cases of overt hypothyroidism but this could probably be attributed to the small sample size. Other studies determining the association of Metabolic Syndrome with thyroid dysfunction found more subjects with subclinical hypothyroidism rather than with overt hypothyroidism amongst the subjects with metabolic syndrome. [19], [20], [21] Numerous studies have found the proportion of female subjects having subclinical thyroid dysfunction to be higher than male subjects with subclinical thyroid dysfunction. [19], [20], [21] The present study also had the same finding.

Waist circumference, mean systolic pressure, diastolic pressure, fasting blood sugar, total cholesterol, LDL and triglycerides, in the present study, were significantly higher in the Metabolic Syndrome group compared to the control group. HDL was significantly lower in cases. These findings are consistent with other studies. [15], [16], [19], [20], [21]

Thyroid function was assessed in the subjects using TSH, fT3 and fT4 assay. Serum fT3 was significantly lower in the Metabolic Syndrome group ($p = 0.014$) than in the control group. Serum TSH was significantly higher in the Metabolic Syndrome group than in the control group ($p< 0.001$). Free T4 was lower in the control group with a p value of 0.259. These findings were similar to those obtained in a study done in Behrampur, Orissa by Meher et al. [20] The study by Gyawali et al. and by Shantha et al., had similar findings except that fT4 but not fT3 was significantly lower in metabolic syndrome cases than in healthy controls. A significant association of subclinical hypothyroidism with Metabolic Syndrome ($p = 0.02$) was seen in the present study. This is similar to the study by Uzunlulu et al, which showed a significant association of subclinical hypothyroidism and Metabolic Syndrome.[18]

Pearson's correlation coefficient was used to determine the association between serum TSH level and fT4 with various components of metabolic syndrome [Table 2 and 3] [Figure 1 and 2]. TSH had significant positive linear association with waist circumference in the metabolic syndrome group ($p=0.006$) and in healthy controls ($p=0.013$) as did HDL cholesterol that had a significant negative association with TSH in the metabolic syndrome group ($p<0.001$) and in healthy controls ($p=0.036$). Serum TSH had a significant positive association ($p<0.001$) with serum triglycerides only in the metabolic syndrome group. In the present study, in healthy controls, across the normal TSH & fT4 reference range, a statistically significant negative correlation was seen between Serum fT4 and waist circumference and a statistically significant positive correlation was seen between Serum fT4 and HDL. A statistically significant positive correlation was seen between Serum fT4 and serum LDL levels in subjects of metabolic syndrome. Similar to the present study was a study by Zhang et al., undertaken to explore the relationship between serum TSH and components of metabolic syndrome in Chinese adolescents. They found that serum TSH was significantly positively correlated with waist circumference, total cholesterol, serum Triglycerides, Serum LDL and serum triglycerides. In healthy euthyroid individuals Serum TSH was positively associated with total cholesterol, LDL and serum Triglycerides. In the study done by Meher et al., multivariate logistic regression analysis showed an association between BMI and subclinical hypothyroidism and that there was a significant association between subclinical hypothyroidism and metabolic syndrome. [20] Shantha et al., concluded that sub-clinical and overt hypothyroidism was significantly associated with metabolic syndrome patients and there is an association between TSH and fT4 with individual components of metabolic syndrome. [21] Zhang et al. concluded that increased serum TSH in adolescents may be a potential risk factor for metabolic syndrome. [22] A study in Taiwan by Lai et al., investigated the relationship between serum TSH levels and components of metabolic syndrome, concluding that even slight increases in TSH, as in subclinical hypothyroidism, may be a risk factor for metabolic syndrome.[23]

Gyawali et al., did not find a statistically significant correlation between TSH or fT4 with metabolic syndrome components. The same study concluded that the prevalence of subclinical hypothyroidism in subjects of metabolic syndrome was high but there was no relationship between thyroid status and all components of metabolic syndrome. [19] Another study done by Wang et al., found no statistically significant correlation between subclinical hypothyroidism and metabolic syndrome or between serum TSH and metabolic syndrome components. [15]

The outcomes in Subclinical hypothyroidism, defined as a state of increased serum thyroid-stimulating hormone (TSH) levels, with circulating thyroxine (T4) and triiodothyronine (T3) concentrations within the population reference range, is likely to depend on the duration and the degree of elevation of the serum TSH.[18] Metabolic syndrome is a condition characterized by a cluster of metabolic disorders including abdominal obesity, insulin resistance/glucose intolerance, dyslipidemia, and hypertension, all of which increase the cardiovascular risk.[8] Metabolic Syndrome and thyroid dysfunction are interlinked due to the effect of thyroid dysfunction on lipid and glucose metabolism, blood pressure, and cardiovascular dysfunction. There are common features in the pathogenic mechanisms of increased cardiovascular risk in metabolic syndrome and hypothyroidism. Insulin resistance is a fundamental feature of metabolic syndrome.[8] Studies indicate an interplay between thyroid status and insulin sensitivity. Insulin resistance leads to an increased production of hepatic cholesterol and very low density lipoproteins (VLDL) and an increased HDL cholesterol (HDL-C) clearance.[24] Thyroid hormones also play an important role in maintaining an equilibrium in glucose metabolism-insulin agonistic (as seen in muscle) or insulin antagonistic (as seen in liver). In hypothyroidism, it has been suggested that insulin resistance is present mainly at the peripheral tissues.[25] It has also been suggested that insulin resistance augments the deleterious effect of hypothyroidism on the lipid profile. [25] A review by Iwen et al. endorses the fact that there is a major influence of Subclinical Hypothyroidism on all components of Metabolic Syndrome and emphasized the fact that the odds of having Metabolic Syndrome are positively associated with high normal TSH levels. [26], [27] A number of cross-sectional and longitudinal follow-

up studies from Japan have found strong associations between Subclinical thyroid dysfunction and Metabolic syndrome. [28], [29], [30] The present study was undertaken with a small sample size and basic relevant investigations as also a simple statistical analysis. This was due to the fact that the project was an undergraduate research project that was completed keeping in mind logistic and economic issues. A larger sample size, a more indepth statistical analysis and the addition of more investigations would yield more information regarding association of Metabolic syndrome and subclinical thyroid dysfunction. The present study has found that the proportion of subjects with metabolic syndrome having thyroid dysfunction is fairly high. In addition, there is a significant relationship between subclinical thyroid dysfunction and metabolic syndrome and a significant association also exists between TSH across the reference range as well as at levels of subclinical hypothyroidism and Waist circumference, Low density lipoprotein and high density lipoprotein. This may suggest the need for continous monitoring of subjects with metabolic syndrome for subclinical hypothyroidism as well as for the appearance of symptoms of overt hypothyroidism.

Table 1: Baseline characteristics of the study population. All data expressed as mean ± standard deviation. P < 0.05 is statistically significant

Parameter	Metabolic Syndrome Group Cases n= 30	Healthy Controls Group n= 30	p value
Age in years	38.23±8.5	36.23±11.22	0.345
Waist circumference in cms	88.17±9.91	72.55±8.15	<0.001*
Fasting Blood Sugar mg/dL	131.43±53.38	83.63±9.43	<0.001*
Systolic Blood Pressure in mmHg	130.47±7.71	112.10±10.29	<0.001*
Diastolic Blood Pressure in mmHg	83.27±6.45	73.77±6.17	<0.001*
Total Cholesterol mg/dL	205.13±33.32	154.70±37.61	<0.001*
Serum Triglycerides mg/dL	205.90±43.94	128.80±13.35	<0.001*
LDL Cholesterol in mg/dL	124.43±31.2	48.77±14.43	<0.001*
HDL Cholesterol in mg/dL	41.23±6.79	54.27±9.75	<0.001*
Serum TSH µIU/mL	4.16±2.16	2.25±0.79	<0.001*
Serum Free T3 pg/mL	2.59±0.97	3.16±0.75	0.014*
Serum Free T4 ng/dL	1.38±0.37	1.47±0.28	0.259

Table 2: Correlation between components of metabolic syndrome and levels of TSH across the metabolic syndrome group and Control group (Pearson's Correlation coefficient)

Parameter	Metabolic Syndrome Group Cases n= 30		Healthy Controls Group n= 30	
	R	p-Value	R	p-Value
Waist Circumference(WC)	0.491	0.006*	0.446	0.013*
Systolic Blood Pressure (SBP)	0.046	0.811	0.192	0.309
Diastolic Blood Pressure (DBP)	0.048	0.799	0.271	0.147
Fasting Blood Sugar (FBS)	0.046	0.810	0.282	0.132
Serum Triglycerides	0.874	<0.001*	0.365	0.048
Serum High Density Lipoprotein (HDL)	-0.711	<0.001*	-0.385	0.036*
Serum Low Density Lipoprotein (LDL)	0.885	<0.0001*	0.503	0.002*
* denotes significant correlation				

Table 3: Correlation between components of metabolic syndrome and levels of fT4 across the metabolic syndrome group and Control group (Pearson's Correlation coefficient)

Parameter	Metabolic Syndrome Group Cases n= 30		Healthy Controls Group n= 30	
	R	p-Value	R	p-Value
Waist Circumference(WC)	-0.016	0.933	-0.510	0.003*
Systolic Blood Pressure (SBP)	-0.137	0.470	-0.119	0.531
Diastolic Blood Pressure (DBP)	-0.186	0.325	-0.192	0.309
Fasting Blood Sugar (FBS)	-0.190	0.314	0.319	0.085
Serum Triglycerides	0.238	0.204	-0.084	0.658
High Density Lipoprotein (HDL)	-0.301	0.106	0.362	0.049*
Serum Low Density Lipoprotein (LDL)	0.408	0.02*	-0.307	0.09
* denotes significant correlation				

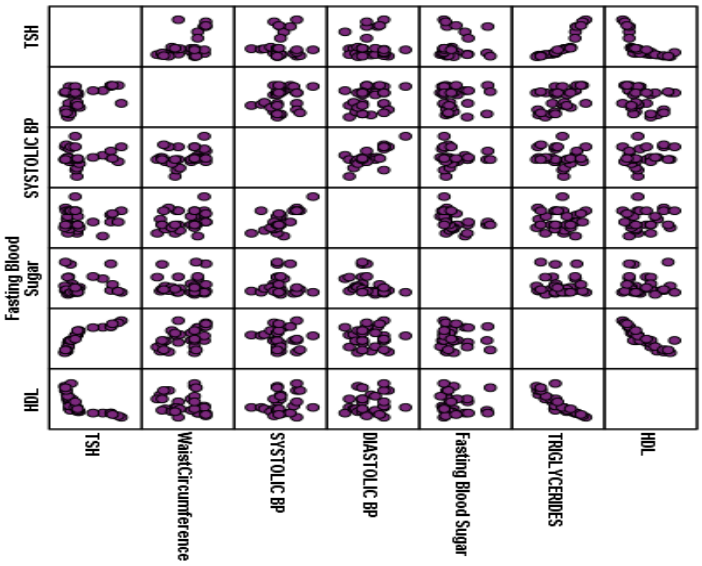

Figure 1: TSH has significant correlation with wait circumference (P<0.01), Triglycerides(P<0.001) & HDL(P<0.001) in MetSyn Cases group.

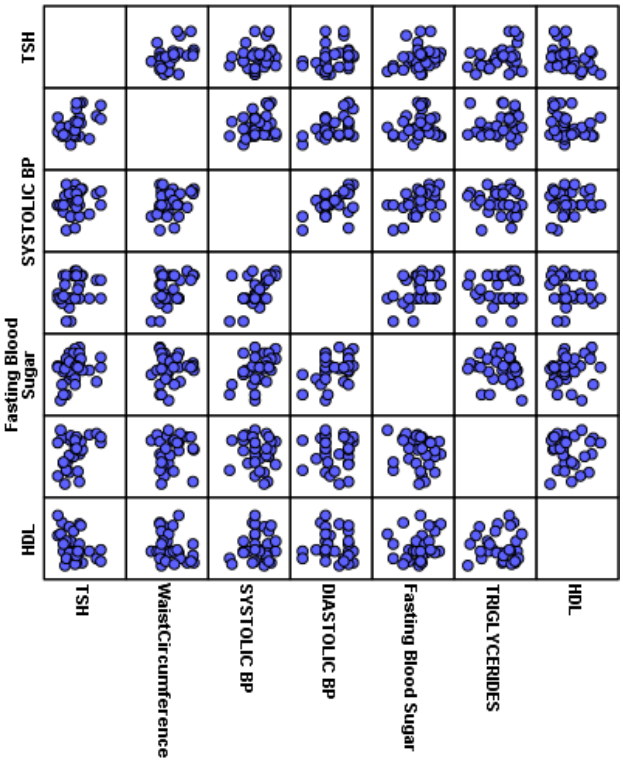

Figure 2: TSH has significant correlation with Waist Circumference (P<0.05)& HDL (P<0.05) in Control group.

References

[1]. Pearce SHS, Brabant G, Duntas LH, et al. 2013 ETA Guideline: Management of Subclinical Hypothyroidism. European Thyroid Journal. 2013;2(4):215-228.
[2]. Jones DD May KE, Geraci SA. Subclinical thyroid disease. Am J Med. 2010 Jun; 123 (6):502-4
[3]. Marwaha RK, Tandon N, Ganie MA, Kanwar R et al. Status of Thyroid Function in Indian Adults: Two Decades After Universal Salt Iodization. JAPI. 2012 April; 60: 32-36
[4]. Grundy SM. Metabolic Syndrome: Connecting and Reconciling Cardiovascular and Diabetes Worlds. J Am Coll Cardiol. 2006;47:1093–100
[5]. Prasad DS, Kabir Z, Dash AK, Das BC. Prevalence and risk factors for metabolic syndrome in Asian Indians: A community study from urban Eastern India. J Cardiovasc Dis Res 2012;3:204-211.
[6]. Vanitha Gowda M N, Krishnamurthy U, Shalini C N , Pruthvish S, Shalini P et al., Metabolic syndrome in an adult population of rural Karnataka. International Journal of Recent Trends in Science & Technology. October 2014; 12(3):483-490.

[7]. Alberti KG, Zimmet PZ: Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus, provisional report of a WHO Consultation. Diabet Med 1998; 15:539- 53.)

[8]. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults.Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) JAMA.2001:285:2486-97

[9]. Kahn R, Buse J, Ferrannini E, Stern M. The Metabolic Syndrome: Time for a Critical Appraisal Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2005; 28:2289-304.

[10]. Backgrounder 1. The IDF consensus worldwide definition of the Metabolic Syndrome. IDF Communications ed. Brussels, Belgium: International Diabetes Federation; 2006.

[11]. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ,Smith SC Jr, Spertus JA, Costa F; American Heart Association; National Heart, Lung, and Blood Institute (2005) Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung and Blood Institute Scientific Statement. Circulation 112: 2735-2752

[12]. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA et al. Harmonizing the Metabolic Syndrome. Circulation 2009;120:1640-5

[13]. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, et al. Consensus Statement for Diagnosis of Obesity, Abdominal Obesity and the Metabolic Syndrome for Asian Indians and Recommendations for Physical Activity, Medical and Surgical Management. JAPI 2009; 57:163- 70.

[14]. Erdogan M, Canataroglu A, Ganidagli S, Kulaksızoglu M.Metabolic syndrome prevalence in subclinical and overt hypothyroid patients and the relation among metabolic syndrome parameters.J Endocrinol Invest. 2011 Jul-Aug;34(7):488-92

[15]. Wang CY, Chang TC, Chen MF. Pei D, Lai CC, Chen YL, Wu CZ, Chang YL, Hsu CH, Pei C, Tang SH. Associations between subclinical thyroid disease and metabolic syndrome. Endocrine Journal. 2012;59(10):1613-4.

[16]. Uzunlulu M, Yorulmaz E, Oguz A. Prevalence of subclinical hypothyroidism in patients with metabolic syndrome.Endocr J. 2007 Feb;54(1):71-76.

[17]. Chugh K, Goyal S, Shankar V, Chugh SN. Thyroid function tests in metabolic syndrome. Indian Journal of Endocrinology and Metabolism. 2012;16(6):958-961.

[18]. Ross DS: Serum thyroid – stimulating hormone measurement for assessment of thyroid function and disease. Endocrinol Metab Clin North Am 2001, 30:245-264.

[19]. Gyawali P, Takanche JS, Shrestha RK, Bhattarai P, Khanal K, Risal P, Koju R. Pattern of Thyroid Dysfunction in Patients with Metabolic Syndrome and Its Relationship with Components of Metabolic Syndrome. Diabetes Metab J. 2015 Feb;39(1):66-73.

[20]. Meher LK, Raveendranathan SK, Kota SK, Sarangi J, Jali SN. Prevalence of hypothyroidism in patients with metabolic syndrome. Thyroid Res Pract 2013;10:60-64.

[21]. Shantha GP, Kumar AA, Jeyachandran V, Rajamanickam D, Rajkumar K, Salim S, et al. Association between primary hypothyroidism and metabolic syndrome and the role of C reactive protein: A crosssectional study from South India. Thyroid Res 2009;2:2.

[22]. Zhang J, Jiang R, Li L, Li P, Li X, Wang Z, et al. Serum thyrotropin is positively correlated with the metabolic syndrome components of obesity and dyslipidemia in chinese adolescents. Int J Endocrinol. 2014;2014:289503. Epub 2014/09/13.

[23]. Lai Y, Wang J, Jiang F, Wang B, Chen Y, Li M, Liu H, Li C, Xue H, Li N, Yu J, Shi L, Bai X, Hou X, Zhu L, Lu L, Wang S, Xing Q, Teng X, Teng W, Shan Z. The relationship between serum thyrotropin and components of metabolic syndrome. Endocr J 2011; 58:23-30.

[24]. Singh BM, Goswami B and Mallika V. Association between insulin resistance and hypothyroidism in females attending a tertiary care hospital. Indian Journal of Clinical Biochemistry, 2010 ; 25 (2) 141-145.

[25]. Gabriela Brenta. Why Can Insulin Resistance Be a Natural Consequence of Thyroid Dysfunction? J of Thyroid Research. 2011;152850:1–9

[26]. Iwen KA, Schroder E, Brabant G. Thyroid hormones and the metabolic syndrome. Eur Thyroid J 2013;2:83-92.

[27]. Taylor PN, Razvi S, Pearce SH, Dayan CM. Clinical review: a review of the clinical consequences of variation in thyroid function within the reference range. J Clin Endocrinol Metab 2013;98:3562-71.

[28]. Nakajima Y, Yamada M, Akuzawa M, Ishii S, Masamura Y, Satoh T, et al. Subclinical hypothyroidism and indices for metabolic syndrome in Japanese women: one-year follow-up study. J Clin Endocrinol Metab 2013;98:3280-7.

[29]. Lee YK, Kim JE, Oh HJ, Park KS, Kim SK, Park SW, et al. Serum TSH level in healthy Koreans and the association of TSH with serum lipid concentration and metabolic syndrome. Korean J Intern Med 2011;26:432-9.

[30]. Oh JY, Sung YA, Lee HJ. Elevated thyroid stimulating hormone levels are associated with metabolic syndrome in euthyroid young women. Korean J Intern Med 2013;28:180-6.