Int J Pharm Bio Sci 2012 July; 3(3): (B) 596 - 603

Research Article **Bio Chemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

PREVALENCE OF THYROID DISORDERS IN COASTAL ANDHRA PRADESH

Ravi Shekhar*[1], V Siva Prabodh[1], NVS Chowdary[1], Desai Vidya[1], MC Das[2]

[1] Department of Biochemistry
[2] Department of Pharmacology
NRI Medical College and General Hospital, Chinakakani, Guntur, Andhra Pradesh, India

ABSTRACT

Objective - To study the prevalence of thyroid dysfunction in post iodization phase and its correlation with dyslipidemia in coastal Andhra Pradesh. Materials and Method – 1330 subjects attending the NRI General Hospital for annual check up from January 2011 to December 2011 were taken into the study. Subjects included into the study were non-smoker, non-alcoholic or without any medication, not undergone thyroidectomy or exposure to radioiodine. The analysis of serum sample collected from subjects was performed on Dade Behring for lipid profile and Centaur CP for thyroid profile. The subjects were divided into 4 groups on the TSH level obtained. Results- In the thyroid disorders, prevalence of overt hypothyroidism was 31.3%, subclinical hypothyroidism was 50 %, and overt hyperthyroid was 18.7%.Discussion – Positive correlation was observed between TSH and Total Cholesterol.

KEYWORDS: TSH, Cholesterol, Dyslipidemia

Ravi Shekhar
Department of Biochemistry NRI Medical College and General Hospital, Chinakakani, Guntur, Andhra Pradesh, India

**Corresponding author*

INTRODUCTION

Iodine is an essential micronutrients required for optimal functioning of thyroid gland and central nervous system[1]. Iodine is required for the synthesis of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3). Iodine deficiency is most important preventable cause of thyroid disorder, brain damage and mental retardation. Iodine deficiency can be prevented by ensuring that the population has as adequate intake of iodine. Consumption of crops and plants grown on iodine deficient soils leads to iodine deficiency in population solely dependent on this vegetation for their iodine requirement. The Government of India launched National Goitre Control Programme in 1962 and in 1992 it was renamed as National Iodine Deficiency Disorders Control Programme to cover a wide spectrum of Iodine Deficiency Disorder (IDD). The objective of the programme were to assess the magnitude of the IDD, supply of iodised salt in place of common salt and resurveys to assess the impact of iodised salt every 5 years[2]. Government of India has banned the sale of non iodated salt in the entire country for direct human consumption under prevention of Food Adulteration Act, 1954 with effect from 17th May 2006[3].

In spite of iodine replacement, goitre is still prevalent in most states of India. The cause of the thyroid disorders may be other goitrogens or deficiency of other micronutrients. Iodine as an immunogen in prevalence of autoimmune thyroid disorders in India is a contentious issue. May be an important cause of thyroid disorder in post iodization phase[1,3].

There are several studies on thyroid disorder but the prevalence varies because it depends upon the subject group and the diagnostic criteria used. The classification of patients with thyroid dysfunction has undergone dramatic changes with the improvement in the methods of analysis. Thyroid disorder has a range of non specific symptoms resulting in delayed diagnosis. Symptoms involving the nervous, cardio-vascular, and gastrointestinal systems have an important impact on health and behaviour. Hyperthyroidism can exist with goitre, ophthalmopathy, and signs of sympathetic nervous system hyper-activity. Fatigue, constipation, dry skin, and poor concentration, may be confused with symptoms of aging as these symptoms are similar to hypothyroidism[4]. Thyroid hormones influence all major metabolic pathways-carbohydrate, proteins and lipids. The thyroid disorders are more prone to affect the lipid metabolism[5]. Hyperthyroidism and hypothyroidism together account for considerable morbidity. The symptoms are insufficient to establish the diagnosis clinically, the biochemical confirmation is required. Screening detects previously unsuspected thyroid dysfunction. American Academy of clinical endocrinologist state that a sensitive TSH test should be used as standard criteria for screening[6,7,8].

MATERIALS AND METHODS

The cross sectional hospital based study included 1330 subjects attending NRI General Hospital, Guntur from July 2010 to June 2011 for annual check up from coastal Andhra Pradesh. The study protocol was approved by the institutional ethics committee and informed consent was obtained from all the subjects. The subjects fulfilling the following criteria were included into the study: non-smokers, non-alcoholics or not on any medication. Subjects with renal, hepatic or pancreatic disorder, diabetes mellitus or undergone thyroidectomy, old patients of thyroid disorders, any exposure to radioiodine or familial hypercholesterolemia were excluded. The subjects in the study group were grouped on the TSH levels. TSH levels upto 0.35μIU/ml was taken as hyper thyroid. TSH values from 0.36μIU/ml to 5.4μIU/ml were considered as euthyroid. TSH levels between 5.5μIU/ml and 10μIU/ml were analyzed for FT_4 for diagnosing it as subclinical hypothyroidism. TSH above 10μIU/ml was considered as hypothyroid.

Under aseptic condition, 5 ml venous blood sample was collected from ante-cubital vein into clot activator vacutainers after overnight fast. The samples were centrifuged at 2500 rpm for 10 minutes. Serum was separated and was analyzed within 2 hours of collection for lipid and thyroid profile. Lipid profile included Total Cholesterol, Triglyceride and HDL. Thyroid profile included T_3, T_4, FT_4 and TSH. Lipid profile was analyzed using Siemens Dimension clinical chemistry flex reagent cartridge on Dade Behring Rx Max auto-analyzer. T_3, T_4, FT_4 and TSH was analysed on Siemens Centaur CP immunoassay auto-analyzer with Centaur CP kits by chemiluminescence method. Bio-Rad internal and external quality controls were used to check the accuracy of results obtained.

RESULTS

The 1330 subjects included 781 (58.7%) males and 549 (41.3%) females. The age group of the subjects ranged from 17 to 85 years. The screened subjects taken in the study were grouped into hypothyroid, subclinical hypothyroid, euthyroid and overt hyperthyroid based on their TSH levels. There were 72 subjects in overt hypothyroid group consisting of 33 males and 39 females. 115 subjects, 55 males and 60 females, were in subclinical hypothyroid group. Euthyroid had 1100 subjects, 678 males and 422 females. Overt hyperthyroid had 43 subjects of which 15 were males and 28 were females. The prevalence of overt hypothyroid, subclinical hypothyroid and hyperthyroid in thyroid disorders was 31.3 %, 50.0 % and 18.7 % respectively. Regression analysis was performed and regression line was drawn using MS office 2007.

Table 1: The comparison of mean among euthyroid with overt hypothyroid, subclinical hypothyroid and overt hyperthyroid was analyzed for Age, T_3, T_4, TSH, Total Cholesterol and HDL

Table 2: Comparison of difference of means between euthyroid and other thyroid disorders

Table 1
Mean and Standard Deviation

	Mean ± SD							
	Age (Male)	Age (Female)	T3	T4	TSH	Total Cholesterol	HDL	LDL
Overt Hypothyroid	52.78 ± 9.96	47.87 ± 11.12	0.92 ± 0.34	6.58 ± 2.43	33.84 ± 39.76	216.77 ± 31.62	43.5 ± 9.25	137.37 ± 28.5
Subclinical Hypothroid	50.61 ± 10.77	47 ± 9.64	1.07 ± 0.33	8.12 ± 2.32	7.18 ± 1.13	190.49 ± 38.38	41.27 ± 10.44	115.5 ± 35.3
Euthyroid	50.06 ± 11.29	49.89 ± 11.01	1.09 ± 0.60	8.95 ± 1.86	2.45 ± 1.13	177.22 ± 33.59	49.99 ± 11.19	99.87 ± 33.86
Hyperthyroid	55.67 ± 9.01	55.89 ± 10.63	5.04 ± 3.48	19.23 ± 5.20	0.09 ± 0.11	156.41 ± 31.49	41.48 ± 10.27	90.4 ± 32.7

Table 2
Comparison of difference of means between euthyroid and other thyroid disorders

	T3	T4	TSH	T Chol	HDL
	P-Value	P-Value	P-Value	P-Value	P-Value
Hypothyroid	0.04	0.001	0.001	<0.001	0.01
Subclinical	NS	0.01	<0.00001	0.01	0.001
Hyperthyroid	0.001	0.0001	<0.000001	0.01	0.01

Table 3
R^2 (TSH and Total Cholesterol in different thyroid disorders)

R^2 (TSH to Serum Cholesterol)			
Euthyroid	Subclinical Hypothyroid	Overt Hypothyroid	Overt Hyperthyroid
0.0025	0.0672	0.0366	0.0522

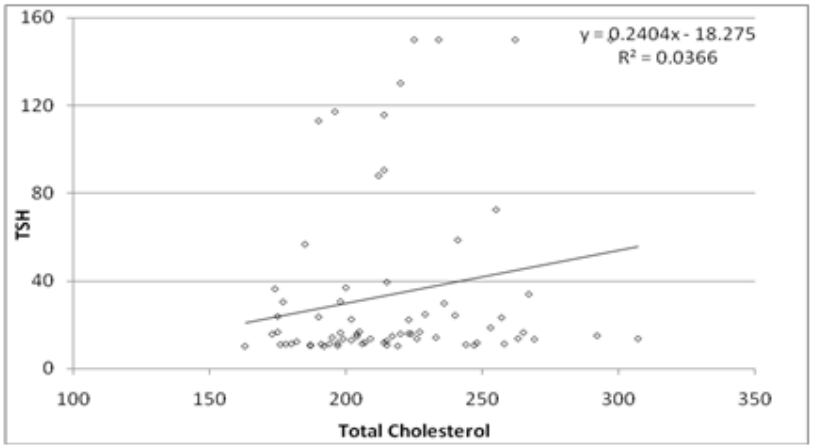

Figure 1
Correlation between TSH and Total Cholesterol in Overt Hypothyroid subjects

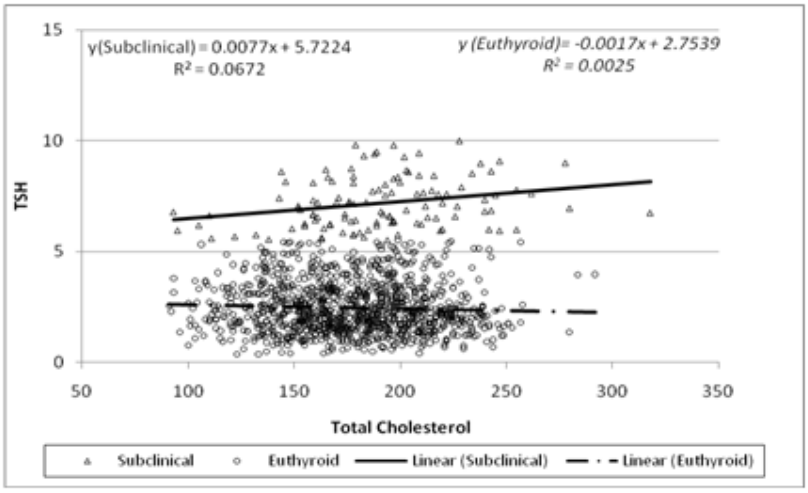

Figure 2
Correlation between TSH and Total Cholesterol in Euthyroid and Subclinical Hypothyroid subjects

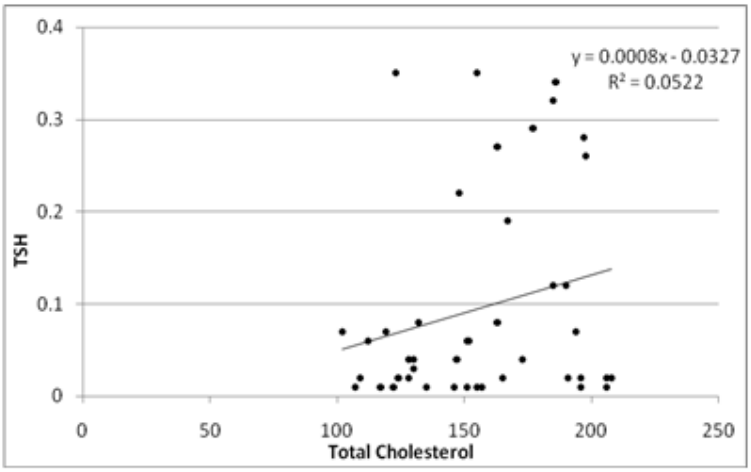

Figure 3
Correlation between TSH and Total Cholesterol in Overt Hyperthyroid Subjects

DISCUSSION

Thyroid disorder is one of the chronic non-communicable diseases being delayed diagnosed as it presents with vague symptoms. In India, thyroid disorders are in a transition zone from a predominantly iodine deficient nation to iodine sufficient population. On the basis of countrywide study, it is estimated that approximate 42 million are having thyroid disease in the post salt-iodization phase[3]. The environmental factors influence the spectrum and the prevalence of thyroid disorders. Deficient iodine intake is known goitrogen. Other unknown goitrogens like protein energy malnutrition, vitamin A, cyanide, iron, selenium and zinc deficiency or their combination may be responsible cause. The high degree of goitre could also be related to the genetic background, possibly due to a high degree of consanguity[8]. Many staple foods consumed in our country contain cyanogenic glucosides that can liberate cyanide. Cyanide is converted to thiocyanates in the body. This is a goitrogen as it blocks the uptake of iodine by the thyroid[9]. Selenium as a

causative factor for goitre formation has been explained by diminished activity of selenocysteine enzymes. In thyroid gland, glutathione peroxidise and deiodinase type I, catalyzes the conversion of thyroxine to triiodothyronine[1,10,11]. In iodine sufficient population, iron deficiency impairs thyroid hormone metabolism because the two steps in thyroid hormone synthesis are catalyzed by thyroperoxidases which are iron requiring enzymes. Iron deficiency lowers plasma T_3 and T_4 concentrations, reduces the rate of conversion of T_4 to T_3 and increase thyrotropin concentrations. Because of these impairments in iodine metabolism, goitre in anaemic individuals may be less responsive to iodine treatment[1,10].

Thyroid hormone is involved in many metabolic pathways, thus presents with multiple symptoms. It has a varying influence on all aspects of lipid metabolism including synthesis, mobilization and degradation. Cholesterol synthesis is stimulated by inducing 3-OH-3-methyl glutaryl coenzyme A reductase in the liver. Thyroid hormone effects lipoprotein lipase activity and thus the hydrolysis of triglyceride in very low density lipoproteins [VLDL] and chylomicrons into fatty acids and glycerol[12].

In the present study, the prevalence of thyroid disorders was found higher in females, which was similar to Whickham study[7], Colorado study[13] and Pescopagano survey[14]. In post menopausal women, there is a decrease in lipolysis and increase in lipo-synthesis, due to a natural depletion of estrogenic hormone formation that characterises a greater quantity of substrate because of cholesterol synthesis[15]. In the present study, elevated TSH levels increased with advancing age of the subjects, similar finding was observed in few studies[4,16,17].

In the present study, total cholesterol, LDL, and triglyceride levels rose with significant trends across grades of thyroid function**.** The overt hypothyroid individuals had an elevated lipid levels which was in accordance with Colorado Study[13] and HUNT study[18]. The overt hypothyroidism has tendency to cause cardiovascular disease and arteriosclerosis by increasing the total cholesterol and LDL.

In the present study, increase in total cholesterol and LDL is also observed in subclinical hypothyroidism. In few studies a modest rise in TSH was shown to correspondent to changes in cholesterol levels affecting cardiovascular outcomes. In Rotterdam study increased incidence of atherosclerosis and myocardial infarction was observed in elderly women[19,20]. But subclinical hypothyroid causing cardiovascular disease is contradictory. Whickham survey found no relationship between initial TSH levels and development of ischemic heart disease[6,20].

Thyroid hormones increase the expression of the cell surface LDL receptors, thus leading to LDL clearance from the serum. In hypothyroidism, the depletion of the thyroid hormones leads to a reduced number of LDL receptors in the liver thereby decreasing the biliary excretion of cholesterol and thus resulting in elevated serum LDL and VLDL levels. It also decreases the lipoprotein lipase activity and causes hypertriglyceridemia[21].

In human plasma, thyroid hormones are transported primarily by T_4 binding prealbumin, serum albumin and T_4 binding globulin. A small fraction of T_4 is bound to plasma lipoprotein. T_3 binds to same proteins, but with a lower affinity. T_4-LDL complex is recognized by LDL receptor and allows T_4 entry into cells. Thyroid hormones increase the expression of the cell surface LDL receptors, thus protects LDL from oxidation. LDL oxidation is common in hypothyroid state as less T_4 is available to bind to LDL and protects it from oxidation by free radicals. Increased risk of atherosclerosis in hypothyroidism is thought to be due to elevated cholesterol levels. LDL plays an important role in CVD development. Decreased thyroid function not only increases the number of LDL particles, but also promotes LDL oxidability[22].

In the present study, HDL did not show variations in thyroid disorders. The relationship between thyroid function and HDL was contradictory. Carantoni et al[23] reported that HDL decrease with hypothyroidism and contributes to the risk of cardiovascular disease. Some studies have reported that HDL is reduced in hyperthyroidism[24].

In the present study, hyperthyroid subjects had the total cholesterol in normal reference range**,** but LDL was decreased similar finding was observed in studies of Jung et al[14], Sundaram et al.[16]. In hyperthyroidism, despite the increased activity of HMG CoA reductase levels of total cholesterol & LDL tend to decrease in subjects. This is due to increased LDL receptor gene expression resulting in enhanced LDL receptor mediated catabolism of LDL particles[21]. Hyperthyroidism results in enhanced LDL oxidability. Cardiovascular manifestations frequent with hyperthyroid are arrhythmia or congestive heart failure secondary to the hypermetabolic state. Angina and precipitation of myocardial infarction could relate to the oxidative modification of LDL by free radicals which could cause changes in endothelium dependent relaxation factor[22]. Atrial fibrillation is the most common complication of hyperthyroid[20].

CONCLUSION

National iodine deficiency disorders control programme helped to minimise the subjects seen with large goitre. In the post-iodization phase despite iodization, the prevalence of goitre has not dramatically declined. Iodine deficiency disorder is a nutritional deficiency resulting from deficiency of iodine in soil and water. Thus, re-emergence can occur inspite of its elimination. Other factors influencing thyroid hormone synthesis has to be studied. The screening is cost effective measure for thyroid dysfunction.

REFERENCES

1. Das S, Bhansali A, Dutta P, Aggarwal A, Bansal MP, Garg D, Ravikiran M, Walia R, Upreti V, Ramakrishnan S, Sachdeva N, Bhadada. Persistence of goiter in the post-iodization phase: micronutrients deficiency or thyroid autoimmunity? *Indian J Med Res*, 133: 103-109, (2011).
2. Kapil U. Successful effort toward elimination Iodine Deficiency Disorders in India. *Indian J Community Med*, 35: 455-468, (2010).
3. Available at http://www.japi.org/thyroid_special_jan_issue_2011/editoral_think%20thyroid.pdf accessed on 15-3-2012
4. Bensenor IM, Goulart AC, Lotufo PA, Menezes PR, Scazufca M. Prevalence of thyroid disorders among older people: results from the Sao Paulo ageing & healthy study. *Cad Saude Publica*, 27: 155-161, (2011).
5. Pucci E, Chiovato L, Pinchera A. Thyroid and lipid metabolism. *International journal of obesity*, 24: S109-S112, (2000).
6. Helfand M, Redfern CC, Sox HC. Screening for thyroid disease. *Ann Intern Med*, 129: 141-143, (1998).
7. Helfand M, Redfern CC. Screening for thyroid disease: An update. *Ann Intern Med*, 129: 144-158, (1998).
8. Baskin HJ, Cobin RH, Duick DS, Gharib H, Guttler RB, Kaplan MM, Segal RL. American association of clinical endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocr Pract*, 8: 457-469, (2002).
9. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. *Indian Journal of Endocrinology Metabolism*, 15: S78-S81, (2011).
10. Hashemipour M, Amini M, Aminorroaya A, Dastjerdi MS, Rezvanian H, Kachoei A, Moaddab MH, Mohammadi M, Kelishadi R, Amini Z, Haghighi S, Moradie FS. High prevalence of goiter in an iodine replete area: do thyroid auto-antibodies play a role? *Asia Pac J Clin Nutr*, 16: 403-410, (2007).
11. Sher L. Role of thyroid hormones in the effects of selenium on mood, behaviour and cognitive function. *Medical Hypothesis*, 57: 480-483, (2001).

12. Peppa M, Betsi G, Dimitriadis G. Lipid abnormalities and cardiometabolic risk in patients with overt and subclinical thyroid disease. *Journal of lipids* 2011, Article ID 575840, 9 pages, doi: 10.1155/2011/575840.
13. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The colorado thyroid disease prevalence study. *Arch Intern Med*, 160: 526-534, (2000).
14. Aghini-Lombardi F, , Antonangeli L,Martoni E, Vitti P, Maccherini D, Leoli F, Rago T, Grasso L, Valeriano R, Balestrieri A, Pinchera A The Spectrum of Thyroid Disorders in an Iodine-Deficient Community: The Pescopagano Survey**.** *J Clin Endocrinol Metab*, 84**:** 561–566, (1999).
15. Maugeri D, Santangelo A, Barbagallo P, Malaguarnera M, Rizza I, Speciale S, Tomarchio M Curasi MP, Panebianco P. Thyroid hormones and lipid metabolism in a group of patients who were over seventy. *Eur Rev Med Pharmacol Sci*, 3:211-216 (1999).
16. Jung CH, Sung K C, Shin HS, RheeEJ, Lee WY, Kim BS, Kang JH, Kim H, Kim SW, Lee MH, Park JR, Kim SW. thyroid dysfunction and their relation to cardiovascular risk factors such as lipid profile, hs CRP and waist Hip ratio in Korea. *The Korean Journal Of Internal Medicine*, 18: 146-153, (2003).
17. Peeters RP. Thyroid hormones and aging. *Hormones*, 7: 28-35 (2008).
18. Asvold BO, Vatten LJ, Nilsen TIL, Bjoro T. The association between TSH within the reference range and serum lipid concentrations in a population-based study. The HUNT study. *European Journal of Endocrinology*, 156:181-186, (2007).
19. Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an in-dependent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam study. *Ann Intern Med*, 132: 270-278, (2000).
20. Helfand M. screening for subclinical thyroid dysfunction in nonpregnant adults: a summary of evidence for the US preventive services task force. *Ann Intern Med*, 140: 128-141, (2004).
21. Liberopoulos EN, Elisaf MS. Dyslipidemia in patients with thyroid disorders. *Hormones*, 1: 218-223, (2002).
22. Sundaram V, Hanna AN, Koneru L, Newman HAI, Falko JM. Both hypothyroidism and hyperthyroidism enhance low density lipoprotein oxidation. *JCE&M*, 82: 3421-3424, (1997).
23**.** Carantoni M, Vigna GB, Stucci N, Zanca R, Fellin R. Low levels of HDL cholesterol in hypothyroid patients with cardiovascular diseases. *Minerva Endocrinol*, 22: 91-7, (1997).
24. Abrams JJ, Grundy SM. Cholesterol metabolism in hypothyroidism and hyperthyroidism in man. *J Lipid Res*, 22: 323-338, (1981)