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The Study Of Lipid Profile Levels, Oxidative Stress And Thyroid Status In Thyroid Disorders

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ABSTRAT

AIM: The study was undertaken to evaluate the interaction between thyroid hormones, the lipid profile levels and role of oxidative stress in patients with thyroid disorders.

MATERIALS AND METHODS: The study includes 25controls with normal thyroid status and 30 hypothyroid cases and 20 hyperthyroid cases having duration of disease below 5years in the age group of 30 to 60 years. Thyroid status was estimated by ELISA method. Ascorbic acid by dinitrophenyl hydrazine method, cholesterol & HDL-C by CHOD-POD method, triglycerides by GPO-POD method.

RESULTS: In hypothyroidism, lipid profile levels are significantly increased and there is decrease in F T_3, F T_4 and increase in TSH. In hyperthyroidism lipid profile levels are not significantly changed and increased F T_3, F T_4 and decreased TSH levels are observed. Both hypo and hyperthyroidism are characterized by higher levels of lipid peroxide when compared with control indicating oxidative damage.

CONCLUSION: In hypothyroidism the increase in lipid peroxide was due to increase in TSH levels, and hypercholesterolemia has a stronger influence on development of oxidative stress. In hyperthyroidism the increase in lipid peroxide was due to increase in

F T_4 levels

INTRODUCTION:

Thyroid hormones synthesized from the thyroid gland are necessary for the normal development of body organs .Thyroid hormones are involved in the regulation of basal metabolic state and in oxidative metabolism [1]. Thyroid problems can be characterized as production of either increased / decreased of hormone that regulates the body metabolism. When the thyroid becomes overactive and releases too much T3, it leads to thyrotoxicosis/hyperthyroidism. Hypothyroidism is a increase in serum TSH level and decrease in

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T3 and T4 levels. Hyperthyroidism cases is lower (2.2%) compared with hypothyroidism in the general population [(2)]. Alterations in the function of Thyroid gland will lead to the changes in serum lipids causing Dyslipidaemia i.e Characterized by increased total cholesterol, triglycerides and LDL-cholesterol levels and decreased HDL-cholesterol levels[(3)].

Thyroid hormones are associated with the oxidative and antioxidative status. The previous studies showed that a significant changes in T3, T4 and TSH level during different thyroid state with different stressors, indicating the relationship between the level of thyroxin and oxidative stress Venditti P .,et.,al [4]. The present study was undertaken to determine whether hyperthyroidism and hypothyroidism have any effect on lipid profile and on the oxidative stress of the body.

MATERIALS AND METHODS

The study was conducted over a period of one year. The study was done using thyroid status and oxidative stress parameters among the subjects with thyroid disorders. The study includes 50 thyroid subjects of which 30 hypothyroid and 20 hyperthyroid patients admitted in general medicine and surgery departments in Narayana hospital, Nellore, Andhra Pradesh, India, between January 2007 to December 2007. The study was approved by the Institutional Human Ethical Committee (IHEC). Informed verbal consent was obtained from all subjects. The data on family history and personal history were collected through standard questionnaire. They were in the age group of 20-60 years both sexes were included. Thyroid status FT3, FT4, TSH estimated by ELISA method [(5, 6, 7)]. Total cholesterol and HDL-C estimated by CHOD-POD method [(8)] and Tgl by GPO – POD method [(9)]. For determination of oxidative stress Malandialdehyde (MDA) is estimated as oxidants by TBARS (Thiobarbituric acid-reactive substances)[(10)] and Vit-C is estimated as antioxidant by dinitrophenyl hydrazine method (DNP)[(11)].

RESULTS

Our study showed that the levels of MDA is higher in both hypothyroid (6.9±2.6) & hyperthyroid patients (7.06 ±2.4) compared with controls (4.4 ±1.8) and vitamin –C is increased in both hypothyroid (1.3 ±0.5) hyperthyroid patients (1.2± 0.6) compared with controls (0.8 ±0.5)

In hypothyroidism total cholesterol (205.4± 51.08) is increased compared with controls (174.5± 38.7) Tgl (167.0 ±70.7) is increased compared with controls (122.6 ±25.9) & HDL-C(44.9 ±13.8) is decreased compared with controls(39.6 ±10.4).Thyroid status T_3 (1.3± 1.0) is decreased compared with controls (2.6± 0.7) and T_4 (0.9± 0.7) is decreased compared with controls (1.2± 0.4)& TSH(6.4 ±4.6) levels are increased compared with controls(2.3 ±1.3)

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In hyperthyroidism total cholesterol (164.4 ± 20.07) there is no change compared with controls (174.5± 38.7) Triglycerides (121.0 ±17.8) is increased compared with controls (122.6 ±25.9) & HDL-C (38.4 ±7.14) is decreased compared with controls (39.6 ±10.4).Thyroid status T_3 (5.1± 1.5) is decreased compared with controls (2.6± 0.7) and T_4 (2.4± 1.4) is decreased compared with controls (1.2± 0.4) and TSH (0.3 ±0.2) levels are increased compared with controls (2.3 ±1.3)

TABLE: 1

COMAPARIION OF MEAN BETWEEN HYPOTHYROID PATIENTS WITH CONTROLS

Sl.No	Parameter	Hypothyroid		controls		Hypethyroid		P'value
		Mean	S.D	mean	S.D	Mean	S.D	
1.	TGL	167.0	70.7	122.6	25.9	121.06	17.8	0.05
2	CHOL	205.4	51.08	174.5	38.7	164.4	20.07	0.05
3	HDL	44.9	13.8	39.6	10.4	38.4	7.14	0.05
4	MDA	6.9	2.6	4.4	1.8	7.06	2.4	0.05
5	Total Vitamin-C	1.3	0.5	0.8	0.5	1.2	0.6	0.05
6	FT3	1.34	1.03	2.67	0.76	5.1	1.5	0.05
7	FT4	0.98	0.75	1.26	0.43	2.4	1.4	0.05
8	TSH	6.4	4.6	2.32	1.35	0.3	0.2	0.05

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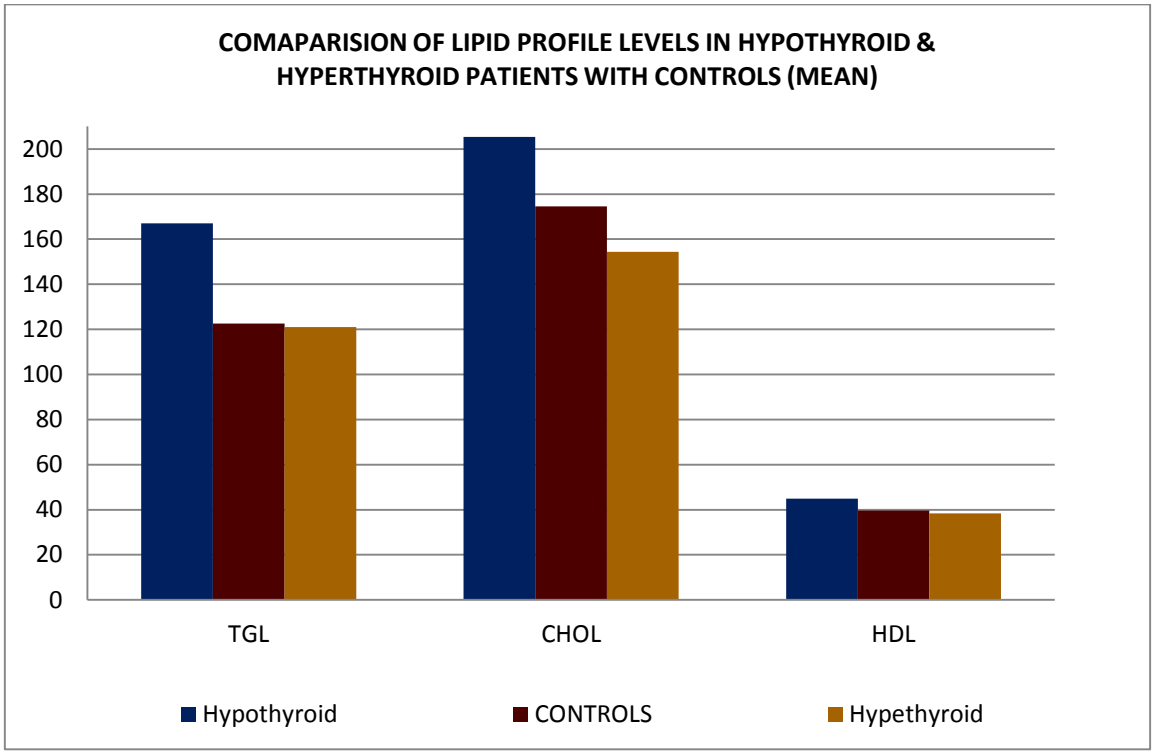

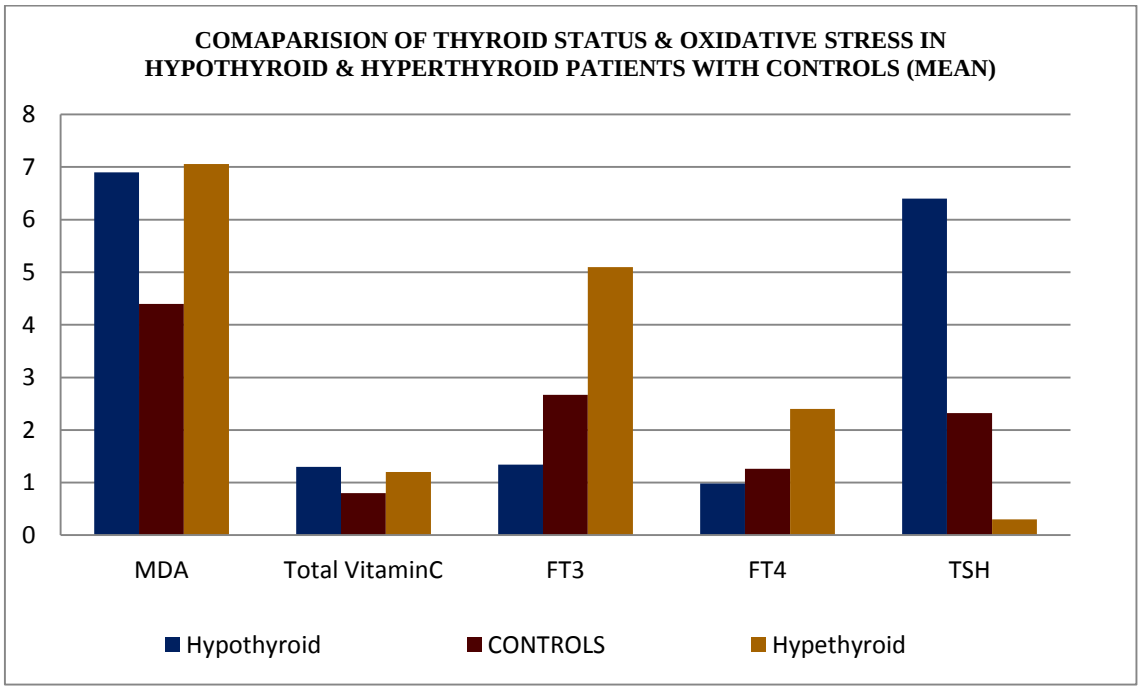

Discussion:

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Fernandez et al. [12] showed that the products of lipid peroxidation were increased in rats that were given triiodothyronine. Dumitriuet al. [13] found high plasma MDA levels in hyperthyroidic patients as opposed to the control group. Costantini et al. [14] demonstrated that hyperthyroidismstimulated lipid peroxidation. Vendittiet al. [15] investigated the effects of hyperthyroidismon lipid peroxidation in rats. Our study shows that there is increased oxidative stress in both hypothyroid and hyperthyroid patients. In hyperthyroidism increased concentrations of thyroid hormones T4 and T3 result in increased basal metabolic rate, increased oxygen consumption and in the production of large quantities of reactive oxygen species which enhance oxidative stress [16]. In hypothyroid the increase in the lipid peroxide is due to high concentration of TSH in plasma. When plasma TSH concentration is high the production of $H_2O_2$is increased. The thyroid is the major site of H2O2 generation and is source of dangerous oxygen radicals generated by fenton reaction. Hydrogen peroxide (H_2O_2) is an important factor for thyroid hormone synthesis. It acts as an acceptor of electrons that are generated during oxidative reactions of hormone synthesis. The production of H_2O_2 in thyroid gland is by NADPH oxidase system in the apical membrane of the thyroid cell. TSH increases H_2O_2 levels through cyclic adenosine 3'5' monophosphate cascade. Increased H_2O_2 levels enhance free radicals which is present in hypothyroidism. Increased amount of free radicals and increased levels of antioxidants, excessive vascularization and H_2O_2 and TSH levels contribute to developing thyroid diseases which lead to oxidative stress.[16]Increase in free radical increases the oxidation of LDL which causes injury to endothelial layer leading to atherosclerosis. [17]

Vitamin-c always forms the first line of antioxidant defense and is the only antioxidant in plasma that can completely prevent lipid peroxidation. Ascorbate act as pro-oxidant because it reduces metal ions leading to production of hydroxyl radical's fromH_2O_2.but biological system like plasma where ascorbate act as an antioxidant even in presence of excess of copper, iron and H_2O_2. [18] In the present study ascorbic acid is increased indicating that effect of oxidative stress on ascorbic acid. Immediately after exposure to an oxidative stress, a decrease is seen in antioxidants capacity using the available anti oxidants, but overtime there may be a response in the tissue, so that an increase in the antioxidants is seen .[19]

Dyslipidemia has been shown to be a common feature of thyroid dysfunction.[20] In Hypothyroidism , Hypercholesterolemia is favoured due to the hormone deficiency also due to the decreased affinity of the lipoprotein lipase. Hypothyroidism increases the oxidation of plasma cholesterol mainly because of (i) an altered pattern of binding and (ii) due to the increased levels of cholesterol, which presents substrate for oxidative

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stress. Thyroid-stimulating hormone has also been shown to induce adipogenesis[20], lipolysis [21]and increase the activity of HMG-CoA [22].Thyroid hormone increases the rate of biosynthesis of cholesterol and also increases the rate of degradation. [14]Even mild elevation of TSH is associated with changes in lipid profile significantly enough to enhance the cardiovascular risk. In hypothyroidism the levels of HDL-Cholesterol remains unaltered. The present study is also consistent with previous study [23] .

The incidence of hyperthyroidism is lower than that of hypothyroidism in the general population (2.2 vs 9.5%)[20] Hyperthyroidism causes decreasing serum lipid concentrations .Increases in metabolism intensity induced by hyperthyroidism cause inappropriate energy expenditure, which results in lipid breakdown as a compensatory measure [24].

CONCLUSION

Oxidative stress plays an important role in thyroid disorders. Increased ROS induced by thyroid hormone leads to an oxidative stress. In hyperthyroidism increased lipid peroxidation is due to increase in FT_4 levels .where as in hypothyroidism it was influenced by increase in TSH levels .Raised antioxidants indicates exhaustion of defending antioxidant. In hypothyroidism the hypercholesterolemia and hypertryglyceridemia is due to increased TSH levels which increases lipase activity. In hyperthyroid subjects the nearly normal values of lipid profile parameters due to balance between lipogenic and lipolytic activity. We can say that altered thyroid states leads to oxidative stress and also oxidative stress may alter the thyroid status. Hence it may be supported that antioxidants may help the patients of altered thyroid status.

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