



## **Study of oxidative stress and lipid profile in hypothyroid patients**

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### **Abstract**

The incidence of hypothyroidism in India is high and it is not adequately controlled. The pathogenesis of hypothyroidism is not very clear, however increased oxidative stress have been reported. Pathological consequences of hypothyroidism point to a high potential for antioxidant imbalance. The present study was carried out to evaluate oxidative stress (MDA, Vitamin C) and to correlate these parameters with the disease process. A total number of 80 subjects comprising of 30 healthy controls and 50 cases studied. Out of 50 patients with hypothyroidism, 30 were subclinical hypothyroid patients and 20 were overt hypothyroid patients. In all the subjects, serum levels of malondialdehyde (MDA) and serum vitamin C were estimated. Serum MDA was significantly increased in overhypothyroidism in comparison to subclinical hypothyroidism and control. The antioxidant serum vitamin C was significantly decreased in overt hypothyroidism when compared to subclinical hypothyroidism and controls. MDA and vitamin c levels correlated with lipid profile explaining the contributory role of oxidative stress and dyslipidemia for the disease process. MDA and serum vitamin C level showed a negative correlation. The presence of increased systemic oxidative stress in hypothyroidism seems to be associated with severity of disease.

**Keywords:** Hypothyroidism, Oxidative Stress, Malonaldehyde (MDA), Serum vitamin C level.

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### **Introduction**

Hypothyroidism, is a common disorder of the endocrine system in which the thyroid gland does not produce enough thyroid hormone.

Worldwide, too little iodine in the diet is the most common cause of hypothyroidism. But, increased free radical production and attenuation of

antioxidant system is currently receiving attention when discussing pathogenesis of hypothyroidism and its complications.

The available data concerning oxidant stress and antioxidant capacity in hypothyroidism are scanty and inconclusive. While some authors suggest

that tissues may be protected from oxidant damage because of a hypometabolic state in hypothyroidism, others report increased oxidative stress in hypothyroidism (Chakrabarti SK et al., 2016).

Oxidative stress plays a pivotal role in cellular injury. Weak defense system of the body becomes unable to counteract the enhanced ROS generation and as a result condition of imbalance between ROS and their protection occurs which leads to domination of the condition of oxidative stress (Halliwell B et al., 2007).

Malondialdehyde is a organic compound with the formula  $CH_2(CHO)_2$ . This reactive species occurs naturally and is a marker for oxidative stress. Reactive oxygen species degrade polyunsaturated lipids present on cell membrane forming malondialdehyde. This aldehyde product is used as a biomarker to measure the level of oxidative stress in an organism (Wikipedia, 2015).

Antioxidants depletion or deficiency may contribute to oxidative stress. Antioxidants not only protect against the direct injurious effects of oxidants, but also alter the inflammatory events that play an important role in the pathogenesis of oxidative stress related diseases.

Vitamin C is a water soluble free radical scavenger, can directly scavenge  $O_2$  and  $OH$ -radicals and help to neutralize physiological oxidant burden created by both exogenous and endogenous sources (Rai et al., 2006).

The present study was conducted with an objective to evaluate the oxidative status and serum lipid profile levels in hypothyroidism & to correlate them with the disease process.

## Materials and Methods

The present study was conducted on 80 subjects of age groups 30- 70 years comprising of 30 healthy age and sex matched healthy control and 50 cases of hypothyroid patients. Out of 50 hypothyroid cases, 30 were subclinical and 20 were overt hypothyroid patients. Controls and cases were selected from a tertiary care hospital in

Uttarakhand, India after obtaining informed consent.

The patients with elevated TSH levels with free T3 & free T4 within normal range were considered as subclinical hypothyroid patients. The patients with elevated TSH level with decreased both free T3 & free T4 levels or either of the two were considered as overt hypothyroid patients.

Patients with diseases like jaundice, renal disease, acute metabolic complications, cardiovascular accidents, acute infections and patients on anti-thyroid/ thyroxine drugs were discarded.

The following tests were done in each sample during the study: (1) Blood urea (2) serum creatinine (3) Serum total Cholesterol (4) Serum HDL & LDL Cholesterol (5) Serum Triglyceride (6) MDA (7) serum vitamin C (8) Complete blood count.

### Estimation of serum malondialdehyde (Satoh, 1978)

Serum malondialdehyde estimated by Kei Satoh Method. It is based on the principle of auto-oxidation of unsaturated fatty acids, involves the formation of semistable peroxides, which then undergo a series of reactions to form malondialdehyde (MDA). MDA reacts with thiobarbituric acid (TBA) to form pink colored chromogen. The resulting chromogen is extracted with 4.0ml of n-butyl alcohol and the absorbance of which is measured at 530 nm.

### Estimation of serum vitamin C (Gunter et al., 1985)

Serum vitamin C was estimated by 2, 4 dinitrophenyl hydrazine method. This method is based on the principle that ascorbic acid is oxidized by copper to form dehydroascorbic acid and diketogulonic acid. These products are treated with 2,4dinitrophenyl hydrazine (DNPH) to form the derivative bis-2,4-dinitrophenyl hydrazone. This compound in strong sulfuric acid, undergoes rearrangement to form a colored product which is measured at 520nm. The reaction is run in the

presence of thiourea to provide a mildly reducing medium, which helps to prevent interference from nonascorbic acid chromogen.

### Estimation of serum lipid profile:

For estimation of total cholesterol and HDL cholesterol CHOD-PAP method which is an enzymatic method were used. Serum triglyceride was estimated by GPO-PAP method. LDL-C & VLDL-C were determined by calculation method.

## Results

**Table 1:** Reference Range

TSH	0.35-4.94	mIU/L
FT3	1.71-3.71	pg/ml
FT4	0.70-1.48	ng/dl

**Table 2:** Clinical data of control, subclinical hypothyroid patients and overt hypothyroid patients (Mean±SD).

Parameters	Control	Subclinical Hypothyroidism	Overt Hypothyroidism
Age(yrs)	41.34 ± 5.37	40.23 ± 5.39	49.34 ± 5.37
Weight(kg)	60.12 ± 4.27	62.34 ± 6.29	63.14 ± 4.20
Body mass index Kg/m <sup>2</sup>	23.49 ± 2.37	23.34 ± 2.14	24.34 ± 2.28
Duration of hypothyroidism(yrs)	nil	8.24 ± 1.27	22.34 ± 2.19

**Table 3:** Biochemical parameters in the study group (Mean±SD)

Parameters	Control	Subclinical Hypothyroidism	Overt Hypothyroidism
Total cholesterol(mg/dl)	158.67±10.11	198.58±15.14**	223.67±23.61**
TAG(mg/dl)	102.59±12.31	126.77±10.50**	150.35±9.51**
HDLc(mg/dl)	44.54±8.51	35.57±14.21*	25.37±12.18*
LDLc(mg/dl)	95.57±7.11	139.57±11.51**	154.67±35.32**

\*p<0.05 \*\*p<0.001

Table 2 is showing clinical profile of study group which is indicating that average age to get hypothyroidism is middle age group (40-50 yrs). Table 3 shows the lipoprotein profile of subclinical hypothyroid, overt hypothyroid cases and healthy controls. Highly significant elevation of total cholesterol (TC), triglyceride (TG) and LDLc has been observed (P<0.001). Significant differences has been noted for HDLc level(p<0.05). There is a relationship between

hypothyroidism and serum lipoprotein abnormalities is well established. (Caselli WP, 1996 & Yeolekar ME,1998). The significant higher serum total cholesterol, LDLc and triglyceride observed among the hypothyroid patients in the current study compared with healthy controls are in agreement with the literature reports that hypothyroidism is one of the risk factor for the onset of coronary heart disease (Halliwell B et al, 1990 & Yilmaz S et al, 2003)

**Table 4** Plasma MDA and Vitamin-C in study groups.

Parameters	Control	Subclinical Hypothyroidism	Overt Hypothyroidism
Plasma MDA(n mol/ml)	2.04±01.16	3.592±10.21*	5.42±09.25**
Plasma Vit. C (mg/ml)	1.02±0.23	0.60±0.08**	0.32±0.002**

\*p&lt;0.05 \*\*p&lt;0.001

Table 4 is showing serum MDA and serum vitamin C level in study groups. MDA level was significantly ( $p<0.05$ ) raised in subclinical hypothyroidism and this difference was highly significant ( $p<0.001$ ) in overt hypothyroidism. Serum vitamin C level difference was highly significant ( $p<0.001$ ) in both cases of subclinical hypothyroidism and overt hypothyroidism when compared to control group.

## Discussion

There is a relationship between hypothyroidism and serum lipoprotein abnormalities is well established (Caselli WP, 1996 & Yeolekar ME, 1998). The significant higher serum total cholesterol, LDLc and triglyceride observed among the hypothyroid patients in the current study compared with healthy controls are in agreement with the literature reports that hypothyroidism is one of the risk factor for the onset of coronary heart disease (Halliwell B et al, 1990 & Yilmaz S et al, 2003)

MDA levels were significantly raised in both the groups of subclinical hypothyroidism and overt hypothyroidism. This explains the generation of free radicals during disease process. vitamin C levels is significantly decreased in both the groups of subclinical and overt hypothyroidism patients. This generation of ROS has been potentiated by

the marked dyslipidemia and increased lipid peroxidation of the disease process (West, 2000).

Thyroid hormone regulates metabolic processes essential for normal growth and development. It also regulates metabolism in the adult (Chakrabarti SK et al, 2016). It is well established that thyroid hormone status correlates with body weight and energy expenditure (Iwen KA et al, 2013). Hypothyroidism-associated oxidative stress is the consequence of both increased production of free radicals and reduced capacity of the anti-oxidative defense (Das K et al, 2004 & Sarandol *et al.*, 2005).

Hyperthyroidism, excess thyroid hormone, promotes a hypermetabolic state characterized by increased resting energy expenditure, weight loss, reduced cholesterol levels, increased lipolysis, and gluconeogenesis (Brent GA; 2008). Conversely, hypothyroidism, reduced thyroid hormone levels, is associated with hypometabolism characterized by reduced resting energy expenditure, weight gain, increased cholesterol levels, reduced lipolysis, and reduced gluconeogenesis (Brent GA, 2012).

Hypothyroidism-induced dysfunction of the respiratory chain in the mitochondria lead to accelerated production of free radicals (i.e., superoxide anion, hydrogen peroxide, and hydroxyl radicals as well as lipid peroxides), which consequently leads to oxidative stress (OS). (Venditti *et al.*, 1997).

Hypothyroidism is generally associated with decreased content of tissue protein. Hypothyroidism also specifically reduces most tissue's cellular thiol reserve and alters glutathione/GSH-PX content. Importantly, SOD is the first line of enzymatic defense against intracellular free radicals. Because of that, a decrease of SOD activity would expose the cell membrane and other components to oxidative damage. Catalase shares with GSH-Px its function of catalyzing the decomposition of H<sub>2</sub>O<sub>2</sub> to water. A low level of catalase activity, then, could primarily damage the endoplasmic reticulum in the cells. Glutathione reductase was little affected by the presence of hypothyroidism (Venditti *et al.*, 1997).

Mitochondria are the favorite targets of thyroid hormones. During thyroid hormone synthesis, there is a constant production of oxygenated water, which is absolutely indispensable for iodine intra follicular oxidation in the presence of thyroid peroxidase. In recent years, the possible correlation between impaired thyroid gland function and reactive oxygen species has been increasingly taken into consideration (Vitale M, 2000).

Screening for lipid profile and oxidative stress can help in overall management of hypothyroidism and can help in prevention of cardiovascular accidents and other complications.

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Sanjay Kumar Varun and K K Kshitiz. (2017). Study of oxidative stress and lipid profile in hypothyroid patients. Int. J. Curr. Res. Med. Sci. 3(3): 56-61.

DOI: <http://dx.doi.org/10.22192/ijcrms.2017.03.03.007>