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Total Antioxidant Capacity and Its Association with Oxidative Stress Markers in Subclinical Hypothyroidism

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Abstract

Hypothyroidism is highly prevalent and affects virtually every organ system. Oxidative stress plays a major role in pathogenesis of overt hypothyroidism and as well as subclinical hypothyroidism. Oxidation is essential for the production of energy in biological system. During the normal metabolic process of producing energy, free radicals are generated. Though free radicals, radical derivatives and non radical reactive species are useful during oxidation but hazardous to living organisms at high concentration and damage all major cellular constituents in our body. Thyroid hormones have well-known effects on mitochondrial oxygen consumption, but how hypothyroidism affects oxidative stress is controversial. So in this view, it is aimed to determine effects of subclinical hypothyroidism through serum malondialdehyde (MDA), carbonyl protein (CP) and total antioxidant capacity (TAC). Serum MDA, CP, TAC, C-reactive protein levels and lipid compositions were studied in 60 subclinical hypothyroid and 60 healthy subjects. MDA and CP were elevated in subclinical hypothyroid patients when compared with controls, while TAC levels show significant decreased between the groups. Oxidative stress in subclinical hypothyroidism determined by increased MDA levels and decreased total antioxidant status. Minimized oxidative stress might be beneficial to prevent other complications in Sub clinical hypothyroidism patients.

Keywords: Malondialdehyde, Carbonyl protein, Total antioxidant capacity, Subclinical hypothyroidism.

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INTRODUCTION

Thyroid disorders are most prevalent in recent decade, especially in the middle aged and elderly women [1]. Subclinical hypothyroidism (SCH) can be defined as a serum thyroid stimulating hormone (TSH) concentration elevated above upper limit of normal range and serum free thyroxine with in reference range. Most of the patients with SCH have no symptoms, on the other hand a few patients have typical symptoms such as weight gain, cold intolerance, constipation which in similar in frequency and similarity to age matched Erythroid control [2]. In adults, SCH is associated with increased risk of progression to overt thyroid disease, abnormal lipid levels, increase risk of atherosclerosis, results in increase cardiovascular morbidity and mortality [3]. Hypothyroidism is the insufficient synthesis of thyroid hormones for metabolic processes throughout the body. Iodine deficiency is the most common causes of primary hypothyroidism, secondary hypothyroidism results from decreased TSH secretion and it also decreases the synthesis of antioxidant enzymes [4].

Oxidative stress results from increased production of ROS or impairment of the antioxidant system. Thyroid hormones have a considerable impact on oxidative stress and oxygen consumption [5]. They are kept in controlled levels in the body via the endocrine negative feedback mechanism. Any changes in their levels could alter redox environment causing changes in the number of activity of mitochondrial respiration chain components resulting in increased generation of ROS with often attenuated by antioxidants [6]. Over production of ROS results in increased O_2 consumption by thyroid hormones which disturbs the pro oxidant / antioxidant balance, leading to oxidative stress and consequent damage to cellular structures, lipids, proteins and DNA [7]. This study was aimed to evaluate the oxidative stress markers and Total Antioxidant Capacity in subclinical hypothyroidism patients and compare it with those of healthy subjects in order to determine the prevalence of this defect in population

MATERIALS AND METHODS:

The study was conducted at ACSR Govt. Medical College, Nellore. The study included 60 subclinical hypothyroid cases attending Medicine and Surgery OPDs and 60 age and sex matched healthy controls selected randomly from different outpatient departments without subclinical hypothyroidism. Based on history, clinical examination and investigations, the subclinical hypothyroid cases suffering from Diabetes Mellitus, Ischemic heart diseases, chronic inflammatory disorders were excluded from the study. Informed consent was taken from known cases and controls and the study is approved by the Institutional Ethical Committee.

About 6ml of venous blood in the Fasting state was collected from both cases and controls with aseptic precautions and the serum separated. Serum Free T_3, Free T_4 and TSH in both cases and controls were measured by Electro chemiluminescence Immuno Assay method. Fasting blood glucose was measured by glucose oxidase method and lipid profile parameters were measured by enzymatic methods, high sensitive CRP was measured by immunoturbidimetric method using semi-automated

Chem 7 analyzer. Total antioxidant capacity was measured by FRAP method & Serum Malondialdehyde (MDA) was measured by spectrophotometric method.

Statistical analysis: The values were expressed as mean ± SD. Means were compared by one way ANOVA using SPSS software version 16 with P value<0.05 as significant.

RESULTS AND DISCUSSION:

The study included 60 controls and 60 Subclinical hypothyroid cases. Of the 60 controls, 38 were males, 22 were females and their mean age was 30.8±7.8 years. Of the 60 cases, 35 were males and 25 were females. The mean age of controls was 31.67±6.5 years. SCH is confirmed by laboratory diagnosis of serum picture of elevated thyroid stimulating hormone and normal serum concentration of free thyroxin and total Tri iodothyronine.

Table.1: Mean ± SD of lipid profile comparison in Controls and SCH patients

Parameter (mg/dl)	Controls n=60	SCH patients (n=60)	P Value
Total Cholesterol (TCl)	167.65±12.10	210±22.85	0.001
HDL Cholesterol (HDL-C)	42.10±6.64	38.99±5.48	0.004
LDL Cholesterol (LDL-C)	102.74±11.67	137.15±20.68	0.001
VLDL (mg/dl)	32.68±3.63	38.79±6.25	0.001
Triacylglycerol (mg/dl)	178.44±22.4	191.64±28.92	0.006

Data are expressed as mean ±SD, p value <0.05 was considered statistically significant.

Table.1 shows serum cholesterol levels (210±22.85), LDL-C (137.15±20.68), VLDL (38.79±6.25) and TG (191.64±28.92) in sub clinical hypothyroidism patients, when compared to control group of serum cholesterol levels (167.65±12.10), LDL-C (102.74±11.67), VLDL (32.68±3.63) and TG (178.44±22.4) respectively increased significantly. The HDL–Cholesterol levels in the control were 42.10±6.64 and in sub clinical hypothyroidism patients was decreased 38.99±5.48 significantly.

Increased serum cholesterol levels, LDL-C, VLDL, TG and decreased levels of HDL Cholesterol are commonly seen in sub clinical hypothyroidism, which generates ROS [8]. The ROS have been reported to induce oxidative damage in membrane lipids, proteins and DNA and might result in cell death by necrosis or apoptosis. The mechanism linking hypo thyroidism with oxidative stress and anti oxidants is unknown [9]

Table 2. Mean ± SD of Inflammatory and oxidative stress markers in Controls and SCH patients

Parameter	Controls n=60	SCH patients (n=60)	P- value
Hs-CRP (mg/dl)	1.37±0.42	3.8±0.82	0.001
S.MDA (µmol/l)	1.7±0.33	2.9±0.4	0.001
Carbonyl protein	19.28±2.34	22.8±3.615	0.001
TAC (µmol/l)	1231.7±89.3	1106.8±63.89	0.001

Hs-CRP = High-sensitive C-reactive protein, **S.MDA**=Serum Malondialdehyde, CP= Carbonyl protein, TAC= Total Antioxidant Capacity. P- Value <0.05 was considered statistically significant.

Table 2 shows, Hs-CRP Mean ± SD (3.8±0.82 mg/L vs 1.37±0.42 mg/L) was significantly higher to SCH group compared with control group. CRP levels elevated are associated with oxidative stress and have a risk of developing cardiovascular disease. Hs-CRP is induced by a specific cytokine; interleukin-6 and marker for assessment of inflammation [10]. Subclinical hypothyroidism (SCH) is at increased risk for cardiovascular disease (CVD). It is not clear whether inflammation is a mechanism intermediary between SCH and CVD [11, 12].

The serum Malondialdehyde (MDA) and Carbonyl protein (CP) levels are significantly increased in SCH patients is 2.9±0.4, 22.8±3.615, when compared to the controls is 1.7±0.33, and 19.28±2.34 respectively shows on Table 2. MDA is an important biomarker of oxidative damage to lipids. MDA is a highly toxic molecule and interaction with DNA and proteins has often been referred to as potentially mutagenic and atherogenic [13 8]. An increased MDA level may alter protein structure and functions. It has been reported that MDA can bind irreversibly to proteins via covalent bonds and may increase the formation of carbonyl protein. The usage of protein CO groups as biomarkers of oxidative stress has some advantages in comparison with the measurement of other oxidation products [14, 15].

Total Antioxidant Capacity in SCH patients (1106.8±63.89) when compared with control (1231.7±89.3) significantly decreased as showed in the table 2. FRAP assay is a novel method of assessing total antioxidant capacity and is considered as a useful indicator of the body's antioxidant status to counteract the oxidative damage due to ROS. Suresh et.al 2009 concluded that, a significantly lower serum TAC concentration in the SCH patients compared to controls reflects a lower total antioxidant capacity [16, 17]. A weakened antioxidant defense system leads to further enhancement in lipid peroxidation. This analysis revealed that both excess TSH and increased MDA levels are mutually influencing elevation of CP and decreased total antioxidant capacity in SCH.

CONCLUSION

The present study shows increased MDA, carbonyl protein concentrations and decreased concentration of total antioxidant capacity, are evident for SCH patients' at asymptomatic stage itself. The possibility of counteracting oxidative stress by a pool of proper antioxidants plus an appropriate diet, mainly in patients whose blood antioxidant deficiencies can be easily rebalanced, may have real health benefit and represent a promising way of inhibiting the progression of disease. Thus, Serum Malondialdehyde, Carbonyl protein and total antioxidant capacity may be useful as an early marker of oxidative stress to monitor and optimize antioxidant therapy as an adjunct in the management of Sub clinical thyroidism patients. So reduction of oxidative stress might be beneficial to prevent other complications in Sub clinical hypothyroidism patients.

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