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*Full Length Research Paper*

# An evaluation of antioxidants and oxidative stress in Iraqi patients with thyroid gland dysfunction

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**The present study evaluates the effects of hypothyroidism and hyperthyroidism states on antioxidant vitamins (A, E, C, β-carotene) and uric acid in Iraqi patients before treatment. Lipid peroxidation, an index of oxidative stress was elevated in hyperthyroidism but reduced in hypothyroidism patients as compared to control. The results showed a highly significant decrease in the sera levels of Vitamins A, E and C in all patients with thyroid dysfunction as compared to control. A highly significant decrease in β-carotene levels in patients with hyperthyroidism and a highly significant increase in β-carotene levels in patients with hypothyroidism were compared to control. The level of uric acid was elevated in hyperthyroidism but reduced in hypothyroidism patients as compared to control. In hypothyroidism patients, there was a significant negative correlation between the levels of thyroid hormones, Vitamins A, E, β-carotene and uric acid with concomitant increase in MDA levels, whereas a significant positive correlation was observed between Vitamin C and MDA levels. In hyperthyroidism patients, there was a significant negative correlation between MDA levels and TT3, β-carotene, Vitamin A, and Vitamin E, while a significant positive correlation with TT4, Vitamin C, and uric acid was found. No changes in TSH were observed. The results of this study reveal the importance of monitoring the levels of those antioxidant vitamins in thyroid dysfunction patients before therapy, especially when the disease is more severe.**

**Key words:** Thyroid gland dysfunction, antioxidant vitamins, lipid peroxidation, oxidative stress.

## INTRODUCTION

Free radicals and disorders of the antioxidant defense system have a pathogenic impact on human tissues and hence are seen as important factors in the development of various diseases (Mahadik et al., 2001; McCord, 2000). Free radicals are atoms, ions or molecules with one or more unpaired electrons in their outer orbits and therefore have an extremely high reactivity. The main free radicals in human tissues are superoxide, hydroxyl, hydrogen peroxide, singlet oxygen, and nitric oxide (Gutteridge, 1995). Free radicals are produced in the normal cell metabolism, in biochemical reactions involving oxygen, for the purpose of destroying bacteria and other living organisms taken into the cell by phagocytosis. However, they may also be overproduced by exposure to radiation, tobacco, and other pollutants or following hyperoxia, excessive exercise, and ischemia.

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Excessive concentration of free radicals in the cell environment may lead to cell damage and death. This damage may be prevented or alleviated by the presence of antioxidant molecules (Patil et al., 2006). Malondialdehyde (MDA) is a natural product of peroxidation of unsaturated fatty acids with three or more double bonds. The interaction between the thyroid hormones and Vitamin A metabolism has long been established (Morley et al., 1978). Vitamin A in plasma binds to a specific protein known as retinol binding protein- RBP, and it has been showed that plasma RBP is complex with the thyroxine binding pre-albumin (Garein and Higueret, 1983). Furthermore, the role of the thyroid hormone in absorption and conversion of carotenoides into Vitamin A is one of the earlier studies pursued (Umesh et al., 1999). In this study, the changes in serum levels of Vitamin A, E, C, β-carotene, and uric acid were determined in hypo- and hyperthyroidism before treatment. The results were correlated with those of MDA in the sera of the corresponding patients. Vitamin E, as

the major chain-broking antioxidant, inhibits lipid peroxidation, thus preventing membrane damage and modification of low density lipoproteins. It is generated by the water soluble Vitamin C. Carotenoids efficiently scavenge singlet molecular oxygen and peroxyl radicals. There is increasing evidence from epidemiological studies, animal experiments, and *in vitro* investigations that an increased intake of antioxidants is associated with a diminished risk for several diseases (Stahl and Sies, 1997). The aim of this study was to investigate the dynamics of oxidative stress and antioxidant status markers in both patients with hypothyroidism and hyperthyroidism before treatment by measuring the level of vitamins (A, E, C, β-carotene) and uric acid in Iraqi patients and then finding the correlation between all these parameters with lipid peroxidation, given by MDA level's determination.

## MATERIALS AND METHODS

### Subjects

Ethical approval (Appendix) was sought and approved by the Ethical Committee of the Chemistry Department, College of Science, Al-Mustansiriya University. We studied patients with newly diagnosed and untreated hypothyroidism (8 males and 27 females), mean aged 44 ± 10 years. A total of 40 patients, 14 males and 26 females (mean aged 41 ± 9 years) with hyperthyroidism were enrolled in this study. A total of 40 healthy volunteers 15 males and 25 females (mean aged 44 ± 11 years) served as controls with normal serum TSH. To eliminate the factors which might affect free radical antioxidant activity, we excluded all smoking and alcohol-drinking subjects, as well as individuals suffering from chronic or acute diseases, such as hypertension, diabetes mellitus, diseases of the liver, kidney, and endocrine and immunological disorders from both patient groups and healthy controls.

### Analysis of samples

Fasting blood samples were collected and placed into containing tubes. After centrifugation at 1500 × g for 5 min the serum were removed and retained for assay of the level of Vitamin C and all the parameters, respectively. Serum samples were stored at 20°C until analysis. Serum concentration of total triiodothyronine (TT3), total thyroxin (TT4) and TSH were measured. Levels of TSH, TT3, and TT4 were measured by mini-VIDIS assay using kit supplied by Biomerieux Marcy-l´Etoile/ France.

### Vitamins A, E, C and β- carotene determination

The method for Vitamin A and β- carotene determination is based on the Neeld-Pearson procedure in which trifluoroacetic acid is reacted with conjugated double bond system of organic solvent extracted compounds to produce a blue color (A620). The results determined from the calibration curve are expressed in mg/dl (McComic, 1986).

Vitamin C determination is based on the oxidation of ascorbic acid in serum by $Cu^{2+}$ to form dehydroascorbic acid that react with the acidic 2,4-dinitrophenylhydrazine to form a red bis-hydrazone which is measured as A520. The level determined from the calibration curve is expressed in mg/dl (McComic, 1986).

The principle of Vitamin E determination is the extraction of tocopherols into hexane after precipitation of proteins with ethanol. Tocopherol is oxidized to tocopherol quinone by the addition of ferric chloride reagent, and the $Fe^{2+}$ in the resultant $FeCl_2$ is complex with α, α - dipyridyl to produce a red color which measured as A510. The results are determined from the calibration curve is expressed in mg/dl (Pesce and Kaplan, 1987).

### Measuring of serum uric acid levels

Uric acid was measured with an enzymatic colorimetric assay using a kit supplied by Giesse Diagnostics, Italy.

### Measuring of serum MDA levels

Malondialdehyde formed from the breakdown of poly unsaturated fatty acids serves as a convenient index of peroxidation reaction. The thiobarbituric acid method of Buege and Aust (1978) was used to measure MDA, which reacts with thiobarbituric acid to yield a pink color. Absorbances were determined at 532 nm.

### Statistical analysis

All data were expressed as mean ± standard deviation (mean ± SD). Statistical analysis was performed using LSD, considering $p < 0.05$ as the lowest limit of significance. Statistical analysis was performed using a software program (SPSS 10 for Windows, USA). One-way analysis of variance (ANOVA) was used to compare means with least significant difference (LSD).

## RESULTS

TT3 displayed highly significant depletion in hypothyroidism patients compared with control group, as shown in Table 1, the results also show a highly significant increase in the levels of TT3 in hyperthyroidism patients compared to control. A similar trend of significance was noticed in the serum level of TT4 in hypothyroidism and hyperthyroidism patients respectively. On the other hand there was a highly significant increase in TSH value of hypothyroidism patients and a significant decrease in hyperthyroidism patients when compared to control group. Table 1 shows that there is no significant difference in the age of both hypothyroidism and hyperthyroidism patients when compared to control group.

Vitamin A shows a highly significant decrease in both hyperthyroidism and hypothyroidism compared with that of control group as shown in Table 2. A similar trend of significance was noticed in the serum level of Vitamins E and C in different groups. A highly significant decrease in serum β-carotene occurs in hyperthyroidism, while a highly significant increase in serum β-carotene in hypothyroidism group as compared with control group, respectively. Also, Table 2 shows a highly significant increase in the levels of serum uric acid and MDA occurs in hyperthyroidism, while a highly significant decrease in hypothyroidism group as compared with control group,

**Table 1.** Thyroid function in patients with hypothyroidism, hyperthyroidism, and controls.

| Group description | Control | Hypothyroidism | P | Hyperthyroidism | P |
|---|---|---|---|---|---|
| No | 40 | 35 | - | 40 | - |
| Mean age (years±SD) | 44±11 | 44±10 | NS | 41±9 | NS |
| Sex ratio (men:women) | 15:25 | 8:27 | - | 14:26 | - |
| $TT_3$ (µmol/L) | 1.635±0.0446 | 0.702±0.274 | <0.0001 | 3.037±0.691 | <0.0001 |
| $TT_4$ (µmol/L) | 90.339±14.147 | 40.128±14.264 | <0.0001 | 166.316±44.430 | <0.0001 |
| TSH (µIU/ml) | 2.084±1.058 | 8.416±2.794 | <0.0001 | 0.191±0.324 | <0.002 |

*NS : Non significant, **the mean difference is significant at the $p < 0.05$ level.

respectively.

Table 3 shows ANOVA analysis and the results of correlation between oxidative stress index (represented by MDA level) and concentration of antioxidant vitamins, and uric acid in hyperthyroidism and hypothyroidism patients.

In hyperthyroidism patients, a highly significant correlations was noticed between MDA and Vitamin E ($P < 0.0001$). Also, a highly significant correlation was observed between MDA and β- carotene ($P < 0.004$), MDA and Vitamin C ($P < 0.007$), MDA and Vitamin A ($P < 0.009$) and MDA and uric acid ($P < 0.019$) while there is a non significant correlation between MDA and thyroid hormones.

In hypothyroidism patients a highly significant correlation was observed between MDA and Vitamin E ($P < 0.006$). Also, a highly significant correlation was observed between MDA and β- carotene ($P < 0.002$), MDA and Vitamin C ($P < 0.014$), MDA and Vitamin A ($P < 0.025$) and MDA and uric acid ($P < 0.012$) while there is only significance between MDA and TSH ($P < 0.05$) but not with other thyroid hormones.

## DISCUSSION

The present study reveal some correlation between thyroid hormones and oxidative stress. Oxidative stress results from an imbalance between formation and neutralization of reactive oxygen species (ROS) / reactive nitrogen species (RNS). Lipid peroxidation reaction leads to formation of MDA (Del Rio et al., 2005). The body has several mechanisms to counteract these attacks by using DNA repair enzymes and /or antioxidants (Pacher et al., 2007; Genestra, 2007; Halliwell, 2007; Willcox et al., 2004). If not regulated properly, oxidative stress can induce a variety of chronic and degenerative disease as well as the aging process and some acute pathologies (Huy et al., 2008). In hyperthyroidism, patients have an increase in TT3 and TT4 and simultaneously decrease of TSH. While the condition was a reverse in hypothyroidism patients, which showed a constant decrease of TT3 and TT4 and simultaneously increase in TSH. Elevated $TT_3$ and $TT_4$ concentrations are indicative of hyperthyroidism and low levels are indicative of hypothyroidism, a low TSH in the presence of elevated thyroid hormones is logical because secretion of TSH from the anterior pituitary is regulated by negative feedback from the serum free thyroid hormone concentration (Stockigt, 2003). Many vitamins, enzymes, organic molecules and trace elements play a major role in scavenging those free radicals generated from food oxidation and many pollutants. Beta-carotene serves as an important antioxidant in keeping cells healthy and also serving as pool that is converted to Vitamin A when needed (Russell, 2004). The results obtained an increase level of β- carotene in patients with hypothyroidism as compared to control group, because individuals with hypothyroidism may lack the carotenoids that is needed to be converted into Vitamin A. Also, the alteration in serum carotene levels found in hypothyroid patients is not the direct consequence of a lack of thyroid hormone in the metabolism of vitamin A, but an indirect effect of thyroid disease. Our results are in good agreement with Umesh et al. (1999). The decreased level of β-carotene in hyperthyroidism as compared to the control group is in agreement with Solati et al. (2007) because of a change in the basal metabolism of this group. Results in Table 2 also showed a highly significant decrease ($p < 0.0001$) in Vitamins A, E and C concentration in both hypothyroidism and hyperthyroidism patients, when a comparison was done with the control group. Vitamin A is a potent antioxidant and acts as a scavenger of free radicals either independently or as a part of large enzyme system. Vitamin A deficiency (VAD) has multiple effects on thyroid function in animals (Arthur et al., 1999):

(1) In the thyroid, VAD decreases thyroidal iodine uptake and iodine incorporation into thyroglobulin and increases thyroid size (Nockles et al., 1984),
(2) In the periphery, VAD increases circulating thyroid hormone concentrations (Morly et al., 1978),
(3) In the pituitary, VA status modulates thyrotropin (thyroid- stimulating hormone) TSH production by Retinoid X receptor (RXR)-mediated expression of pituitary TSHβmRNA (Wolf, 2002).

Clinical and experimental studies showed an elevated

**Table 2.** Serum levels of antioxidant vitamin A, E and C, β- carotene, uric acid, and (MDA) in different cases of thyroid dysfunction.

| Group type (No. of studies) | Component | Mean | SD | SE | P |
|---|---|---|---|---|---|
| (Hyper) (N=40) | | 20.4 | 6.182 | 0.977 | <0.0001 |
| (Hypo) (N=35) | Vit.A (mg/dl) ×10-2 | 21.9 | 4.279 | 0.723 | <0.0001 |
| (C) (N=40) | | 33.4 | 7.534 | 1.19 | - |
| (Hyper) | | 34.7 | 18.5 | 2.92 | <0.0001 |
| (Hypo) | Vit.E (mg/dl) ×10-2 | 66.6 | 18.2 | 3.07 | <0.0001 |
| C | | 109 | 31.5 | 4.99 | - |
| (Hyper) | | 124.4 | 30.1 | 4.77 | <0.0001 |
| (Hypo) | Vit.C (mg/lL) ×10-2 | 134.1 | 44.9 | 7.59 | <0.0001 |
| C | | 146.7 | 49.6 | 7.85 | - |
| (Hyper) | | 11.7 | 1.774 | 0.281 | <0.0001 |
| (Hypo) | β- carotene (mg/dl)×10-2 | 20.2 | 5.766 | 0.975 | <0.0001 |
| C | | 15.7 | 2.037 | 0.322 | - |
| (Hyper) | | 37.6 | 1.91 | 30.2 | <0.0001 |
| (Hypo) | Uric acid (mmol/L) ×10-2 | 20.2 | 2.747 | 46.4 | <0.0001 |
| C | | 25.0 | 1.997 | 31.6 | - |
| (Hyper) | | 163.1 | 18.8 | 2.98 | <0.0001 |
| (Hypo) | MDA (µmol/L) ×10-2 | 81.6 | 20.6 | 3.48 | <0.0001 |
| C | | 108.7 | 13.3 | 2.11 | - |

Hyper: hyperthyroidism, Hypo: hypothyroidism, C: healthy control group

free radical level in hyperthyroidism. Hyperthyroidism is a hyper metabolic state accompanied by an increase in the total consumption of oxygen, fostering formation of reactive oxygen species and other free radicals, or the occurrence of oxidative stress (Abalovich et al., 2003). For these reasons, the antioxidant Vitamin A had been consumed as a result of excessive production of free radicals (Bourdel-Marchasson et al., 2001). Furthermore, it has also been reported recently that hyperthyroidism enhances tumor growth *in vivo* (Ferreira et al., 2007). In light of the present knowledge, this may be attributed not only to the aforementioned oxidative stress, as it is an important factor in cancer etiology (Hussain et al., 2003), but also to the stimulation of glucose turnover observed in patients with hyperthyroidism (Laville and Riou, 1984), as exacerbated glucose consumption is a cancer hallmark (Ferreira, 2010).

Interestingly, Vitamin A decreases tissue responsiveness to thyroxine hormones, as evidenced by downregulation of Na-K-ATPase activity in the liver along with the decrease in size of the thyroid gland (Garcin et al., 1983). Similarly, it has been shown that Vitamin A enhances the conversion of T4 to T3 (Garcin et al., 1983). Our results were in agreement with Solati et al. (2007).

Vitamin E was reported to be an important factor in quenching free radicals and increasing of the capability of the immune system (Ersan et al., 2006). We can extrapolate from the lower Vitamin E level in thyroid dysfunction that a higher rate of free radical metabolism is occurring. Lowered Vitamin E level is presumably due to its use in preventing free radical damage that seems more extensive in thyroid dysfunction patients (Garcin et al., 1983). Mano et al. (1998) found in their study patients with various thyroid disorders that they presented elevated Vitamin E levels in their thyroid tissue. Researchers concluded that Vitamin E acts as a scavenger in thyroid follicular cell dysfunction. Additional studies have demonstrated that active oxygen radicals inhibit the activity of an enzyme responsible for the conversion of T4 to the active hormone T3 and that sufficient Vitamin E levels may mitigate that effect (Brzezinska-Slebodzinska and Pietras, 1997). Vitamin E, as an antioxidant, might have indirectly caused the destruction of $H_2O_2$, the required oxidizing agent for iodide oxidation, thus leading to a decrease in thyroid hormone biosynthesis (Zamora et al., 1991). Our findings are consistent with the past researches that highlighted the importance of the effects of Vitamin E in oxidative stress and as component of the antioxidant defense system (Kumar et al., 1992).

Vitamin C is considered the most powerful natural

**Table 3.** Correlation coefficients and the significant levels of different serum chemical components in patients with hyperthyroidism or hypothyroidism.

| Component vs. MDA | Hyperthyroidism | | | | | Hypothyroidism | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Slope | Intercept | $R^2$ | R | P | Slope | Intercept | $R^2$ | r | P |
| $TT_3$ (µmol/L) | -1.6327 | 6.0904 | 0.1205 | -0.347* | 0.28 | -0.5635 | 1.1393 | 0.118 | -0.334* | 0.43 |
| $TT_4$ (µmol/L) | 106.91 | 5.5299 | 0.1346 | 0.367* | 0.020 | -18.828 | 57.934 | 0.1212 | -0.348* | 0.04 |
| TSH (µIU/ml) | -0.0105 | 0.9594 | 3E-05 | -0.006 | 0.972 | -5.5817 | 13.581 | 0.1125 | -0.335* | 0.05 |
| B-Carotene (mg/dl) | -4.9575 | 2.2193 | 0.1960 | -0.443** | 0.004 | 1.3658 | 0.5232 | 0.2533 | -0.503** | 0.002 |
| Vitamin A (mg/dl) | -1.2308 | 1.8598 | 0.1655 | -0.407** | 0.009 | -1.4921 | 1.1118 | 0.1438 | -0.379* | 0.025 |
| Vitamin E (mg/dl) | -0.5275 | 1.7806 | 0.2899 | -0.538** | 0.0001 | -0.4350 | 1.0666 | 0.2067 | -0.455* | 0.006 |
| Vitamin C (mg/dl) | 0.3051 | 1.2495 | 0.1783 | 0.422** | 0.007 | 0.0915 | 0.6665 | 0.1685 | 0.411* | 0.014 |
| Uric acid (mmol/L) | 1.5356 | 1.1049 | 0.1355 | 0.368* | 0.019 | -1.9988 | 1.1766 | 0.1770 | -0.421* | 0.012 |

*Correlation is significant at the 0.05 level, **correlation is significant at the 0.01 level.

antioxidant (Weber et al., 1996), which is capable of "scavenging" reactive oxygen species by reducing free radicals to more stable species (Gumuslu et al., 2000).

Our results were in good agreement with those obtained by Mohan et al. (2004) and Alicigüzel et al. (2001) as these studies described low levels of Vitamin C in hyperthyroidism and increase oxidative stress at the same time, it also indicate that antioxidant vitamin become oxidized and it is eventually consumed in exerting its antioxidant action. The decrease in serum levels of antioxidant vitamins was greater in Iraqi individuals of thyroid dysfunction in comparison with western population. This can be attributed to nutritional differences among different societies and to the difference in concentration of air, water and food pollutants among those populations.

Uric acid is the major end-product of metabolism of all nitrogen containing compounds. The results show in Table 2, a highly significant increase ($p < 0.0001$) in uric acid concentration in hyperthyroidism patients and a highly significant decrease ($p < 0.0001$) in hypothyroidism patients were detected in comparison with the control group. Uric acid is considered as one of the antioxidants that are directly scavenging oxygen radicals, singlet oxygen, oxo-haem oxidants and hydroxyl radicals. Another important property of uric acid is its ability to inhibit ascorbate oxidation, as well as lipid peroxidation. In contrast to other antioxidant scavenger reactions, the inhibition of ascorbate oxidation and lipid peroxidation provided by uric acid does not involve uric acid oxidation (Davies et al., 1986). The raised concentration of uric acid may be due to increase purine synthesis or increased degradation of puric nucleotides or decreased secretion on the other (Sato et al., 1995). Our results were agreement with Vrca et al. (2004) which found an increased level of uric acid in the serum of patients with hyperthyroidism disease and correlated well with the concentration of thyroid hormones. Also, they found that the concentration of uric acid in the serum of patients with hypothyroidism was lower compared to the control group. The increase concentration of uric acid in hyperthyroidism is a consequence of the response of the organism to oxidative stress and mobilization of protective antioxidative mechanism (Vrca et al., 2004).

A highly significant change in MDA levels in patients with thyroid dysfunction compared with control group was observed in Table 2. It was stated in the several studies that not only hyperthyroidism, but also hypothyroidism led to changes in oxidant and antioxidant systems (Brzezińska-Slebodzińska, 2001). Pathological disorders in thyroid gland bring about functional changes in different organs of the body. Findings obtained in both *in vivo* and *in vitro* studies point out that thyroid hormones have a strong impact on oxidative stress (Rasim et al., 2005).

Table 3 shows a good negative correlation of this component with TT3, TT4, and TSH in hypothyroidism patients, while there was a negative relationship between TT3 and MDA, a positive relationship between TT4 and MDA and no change was observed between TSH and MDA in hyperthyroidism patients. In hypothyroidism, a decrease in free radical production is expected because of the metabolic suppression brought about by the decrement in thyroid hormones levels (Pereira et al., 1994). On the other hand, hyperthyroidism is characterized by an increasing cellular metabolic rate, and thus an increased amount of free radicals (Castitho et al., 1998), and an increase in peroxides levels (Morini et al., 1991). Previous clinical and experimental studies

showed a changed in free radical level (with different results) in hypothyroidism and hyperthyroidism. Some of the studies show a significant increase (Chattopadhyay et al., 2003; Sawant et al., 2003). While some other showed a significant decrease (Yilmaz et al., 2003; Brzezińska-Slebodzińska, 2001), or no significant differences (Dariyerli et al., 2004; Gredilla et al., 2003).

Table 3 reveal the correlation between MDA and Vitamins A, E, C, β- carotene and uric acid in patients with hypothyroidism and hyperthyroidism patients. These correlations represent the direct effect of MDA on antioxidant components level. The results show a positive correlation between MDA and β-carotene in hypothyroidism patients. Our findings indicate that the increased levels of MDA and β- carotene are associated with a reduced thyroid function patients. Many individual with hypothyroidism cannot convert β-carotene to Vitamin A, because β-carotene can quench the singlet oxygen without damage to itself and this can be used over and over gain (Passwater, 1984). This is related with β-carotene structure which consists of a long string of double bound with single bound in between. Thus, β-carotene can absorb the singlet oxygen's energy and speared it throughout this long chain of bonds. β-carotene then releases the energy as heat and returns to its usual state (Gaby and Singh, 1991). Table 3 also shows a negative correlation between MDA and β-carotene in hyperthyroidism patients. This result revealed that increasing the oxidative stress will be increasing the breakdown of the measured carotenoids contributing to the lower circulating concentration found in this study. Indeed, if the major mechanism by which inflammation is reduced breakdown, β-carotene concentration in the present study might then be expected, in that the concentration of β-carotene would be very low (Quasim et al., 2003; Galloway et al., 2000). A significant inverse correlation between MDA and Vitamin A was apparent in Table 3 in both cases, suggesting a deficiency in Vitamin A or its consumption as an antioxidant secondary to the excessive production of free radicals (Marchasson et al., 2001). In the present study, a highly significant inversed linear correlation between MDA and Vitamin E levels, and a significant positive correlation between MDA and Vitamin C levels was recorded in hypothyroidism and hyperthyroidism patients. Vitamins C and E are diet-derived antioxidants of major physiological importance (Krajcovicova-Kudlackova et al., 2004). Vitamin C reacts directly with superoxide, hydroxyl radical and singlet oxygen, and it reduces the tocopherol radical back to α-tocopherol (Hamilton et al., 2000). Vitamin E converts the peroxyl radical to the much less reactive hydroperoxides, thus inhibiting the propagation step in lipid peroxidation (Esterbauer and Ramos, 1995). Newer vitamin research has suggested that antioxidant vitamins, such as Vitamins C and E, can reduce the oxidative stress caused by hypothyroidism (Sarandol and Tas, 2005; Oner and Kukner, 2003). Results in Table 3 show a negative significant correlation between MDA and uric acid levels in hypothyroidism patients, and a positive significant correlation between MDA and uric acid levels in hyperthyroidism patients. The positive correlation may be attributed to the two opposing direction of uric acid production in hyperthyroidism and its consumption (an antioxidant) which lead to a net increase in this variable with increasing in lipid peroxidation status in hyperthyroidism patients. This happens because the enzyme xanthine oxidase shows an enhanced activity with increased lipid peroxidation process caused by enhanced free radical formation together with higher supply of substrates and an insufficient defense antioxidant (Krajcovicova-Kudlackova et al., 2004), which lead to a final increase in the level of the end- product of purine catabolism. It has been suggested that Vitamin E has the potential to inhibit xanthine oxidase, the enzyme involved in urate synthesis (Shaheen et al., 1996).

Finally, from all the aforementioned observations it can be concluded that increased generation of reactive oxygen species and concomitant impairment of the antioxidant system occurs in patients with hyperthyroidism, and particularly in patients with hypothyroidism. These findings indicate that thyroid hormones have a strong impact on oxidative stress and the antioxidant system.

**REFERENCES**


Abalovich M, Liesuy S, Gutierrez S, Repetto M (2003). Peripheral parameters of oxidative strees in Graves's disease: The effect of methimazole and 131 iodine treatment. Clin. Endocrinol., 59(3):321-327.

Alicigüzel Y, Özdem SN, Özdem SS, Karayalcin U, Siedlak SL, Perry G, Smith MA (2001). Erythrocyte, plasma, and serum antioxidant activities in untreated toxic multinodular goiter patients. Free Radic. Biol. Med., 30(6):665-70.

Arthur JR, Beckett M, Mitchell JH (1999). Interactions between selenium and iodine deficiencies in man and animals. Nutr. Res. Rev., 12:55-73.

Brzezińska-Slebodzińska E (2001). Fever induced oxidative stress: the effect of thyroid status and the 5'-monodeiodinase activity, protective role of selenium and vitamin E. J. Physiol. Pharmacol., 52(2): 275-284.

Bourdel-Marchasson I, Delmas Beauvieux MC, Peuchant E, Richard-Harston S, Decamps A, Reignier B, Emeriau JP, Rainfray M (2001). Antioxidant defences and oxidative stress markers in erythrocytes and plasma from normally nourished elderly Alzheimer patients. Age Ageing, 30(3): 235-241.

Brzezinska-Slebodzinska E, Pietras B (1997). The protective role of some antioxidants and scavengers on the free radicals-induced inhibition of the liver iodothyronine 5'-monodeiodinase activity and thiols content. J. Physiol. Pharmacol. 48(3): 451-59.

Buege JA, Aust SD (1978). Microsomal lipid peroxidation. Methods Enzymol., 52: 302-310.

Castitho RF, Kowaltowski AJ, Vercesi AE (1998). 3, 5, 3'-triiodothyronine induces mitochondrial permeability transition mediated by reactive oxygen species and membrane protein thiol oxidation. Arch. Biochem. Biophys. 345(1): 151-57.

Chattopadhyay S, Zaidi G, Das K, Chainy GBN (2003). Effects of hypothyroidism induced by 6-n-propylthiouracil and its reversal by T3 on rat heart superoxide dismutase, catalase and lipid peroxidation. Indian J. Exp. Biol., 41: 846-849.

Dariyerli N, Toplan S, Akyolcu MC, Hatemi H, Yigit G (2004).

Erythrocyte osmotic fragility and oxidative stress in experimental hypothyroidism. Endocrine, 25: 1-5.
Davies KJ, Seranian A, Muakkassah KFS, Hoshhstein P (1986). Uric acid- iron complex. A new aspect of the antioxidant Function of uric acid. Biochem. J., 235: 747-754.
Del Rio D, Stewart AJ, Pellegrini N (2005). A review of recent studies on malondialdehyde as toxic molecule and biological marker of oxidative stress". Nutr. Metab. Cardiovasc. Dis., 15 (4): 316–28.
Ersan S, Bakir S, Ersan EE, Dogan O (2006). Examination of free radical metabolism and antioxidant defense system elements in patients with obsessive-compulsive disorder. Prog. Neuropsychopharmacol. Biol. Psychiatry, 30: 1039-42.
Esterbauer H, Ramos P (1995). Chemistry and pathophysiology of oxidation of LDL. Rev. Physrol. Biochem. Pharmacol., 127: 31-64.
Ferreira E, Estrela da Silva A, Serakides R, Gomes MG , Cassali GD (2007). Ehrlich tumor as model to study artificial hyperthyroidism influence on breast cancer. Pathol. Res. Pract., 203**:** 39-44.
Ferreira LMR (2010). Cancer metabolism: The Warburg effect today. Exp. Mol. Pathol., 89**:** 372-80.
Gaby SK, Singh VN (1991). β-carotene, Vitamin Intake and Health: A Scientific Review, Marcel Dekker.; N.Y., p30.
Galloway P, McMillan DC, Sattar N (2000). Effect of the inflammatory response on trace elements and vitamin status. Ann. Clin. Biochem., 37: 289-97.
Garein H, Higueret P (1983). The thyroid hormones in vitamin A-deficient rats: Effect of retinoic acid supplementation. Ann. Nutr. Metab., 27: 495-500.
Genestra M (2007). Oxyl radicals, redox-sensitive signalling cascades and antioxidants. Cell Signal., 19: 1807-19.
Gredilla R, Lopez Tones M, Portero-Otin M, Pamplona R, Barja G (2003). Influence of hyper and hypothyroidism on lipid peroxidation, unsaturation of phospholipids, glutathione system and oxidative damage to nuclear and mitochondrial DNA in mice skeletal muscle. Acta Vet. Hung., 51: 343-51.
Gumuslu S, Korgun DK, Bilmen S, Yargilcoglu p, Agar A (2000). Effect of sulfur dioxide inhibition on plasma vitamin C and ceruloplasmin in ageing rats. Ind. Health, 38; 319-22.
Gutteridge JMC (1995). Lipid peroxidation and antioxidants as biomarkers of tissue damage. Clin. Chem., 41: 1819–28.
Halliwell B (2007). Biochemistry of oxidative stress. Biochem. Soc. Trans., 35: 1147-50.
Hamilton JMJ, Gilmore WS, Benzie IFF, Mulholland CW, Strain JJ (2000). Interactions between vitamin C and vitamin E in human subjects. Br. J. Nutr., 84: 261-67.
Hussain SP, Hofseth LH, Harris CC (2003). Radical causes of cancer. Nat. Rev. Cancer, 3**:** 276-85.
Huy LAP, He H, Pham-Huy C (2008). Free Radicals, Antioxidants in Disease and Health. Int. J. Biomed. Sci., 4(2): 89-96.
Krajcovicova-Kudlackova M, Paukova M, Dusinska M (2004). Lipid peroxidation in relation to vitamin C and vitamin E levels. Cent. Eur. J. Publ. Health, 12(1): 46-48.
Kumar CT, Reddy VK, Prosad M, Thyagaraju K, Reddanna P (1992). Dietary supplementation of vitamin E protects heart tissue from exercise-induced oxidant stress. Mol. Cell Biochem. 111: 109-15.
Laville M, Riou J (1984). Glucose metabolism in experimental hyperthyroidism: intact in vivo sensitivity to insulin with abnormal binding and increased glucose turnover. J. Clin. Endocrinol. Metab., 58: 960-65.
Mahadik SP, Evans D, Lal H (2001). Oxidative stress and role of antioxidant and omega-3 essential fatty acid supplementation in schizophrenia. Prog Neuropsychopharmacol. Biol. Psychiatry, 25: 463–93.
Marchasson IB, Delmas-Beauvieux MC, Penchan E, Rrchard-Harston S, Decamps A, Reignier B, Emeriau JP, Rainfray M (2001). Antioxidant defences and oxidative stress markers in erythrocytes and plasma from normally nourished elderly Alzheimer patients. Age Ageing, 30: 235-41.
McCord JM (2000). The evolution of free radicals and oxidative stress. Am. J. Med., 108(8): 652–9.
McComic DB (1986). Vitamins. In: Tietz NW, editor.Textbook of clinical chemistry. Philadelphia, PA : WB Saunders Company, pp 932-33, 960-62 .
Mohan KKM, Bobby Z, Selvaraj N, Kumar DA, Chandra KB, Sen SK, Ramesh R, Ranganathan P (2004). Possible link between glycated hemoglobin and lipid peroxidation in hyperthyroidism. Clin. Chim. Acta., 342: 187-92.
Morini P, Casalino E, Sblanco C, Landriscina C (1991). The response of rat liver lipid peroxidation, antioxidant enzyme activities and glutathione concentration of the thyroid hormone. Int. J. Biochem., 23: 1025-30.
Morley JE, Damassa DA, Bordan J, Pekrary AE, Hersham JM (1978). Thyroid function and vitamin A deficiency .Life Sci., 22: 1901-6.
Nockles CF, Ewing DL, Phetteplace H (1984). Hypothyroidisms: an early signs of vitamin A deficiency in chickenes. J. Nutr., 114: 1733-36.
Oner J, Kukner A (2003). Effect of vitamin E on follicular cell proliferation and expression of apoptosis-associated factors in rats with 6-N-propyl-2-thiouracil-induced goitrogenesis. Folia Histochem. Cytobiol., 41(4): 213-217.
Pacher P, Beckman JS, Liaudet L (2007). Nitric oxide and peroxynitrite in health and disease. Physiol. Rev., 87: 315-24.
Passwater RA (1984). Beta Carotene, the Backstage Natnent Now Universally Recognized for cancer prevention. Keats Publishing Inc., New Canaan Conn., p18.
Patil SB, Kodliwadmath MV, Kodliwadmath MV (2006). Lipid peroxidation and nonenzymatic antioxidants in normal pregnancy. J. Obstes. Gynecol. Indian, 56(5): 399-401.
Pereira B, Rosa LF, Safi DA, Bechara EJ, Curi R (1994). Control of superoxide dismutase, catalase and glutathione peroxidase activaties in rat lymphoid organs by thyroid hormones. J. Endocrinol., 140: 73-77.
Pesce AJ, Kaplan LA (1987). Methods in clinical chemistry. St Louis, MO: Mosby Company, p 586-587.
Quasim T, McMillan DC, Talwar D, Sattar N, O'reilly DST, Kinsella J (2003). Lower concentration of carotenoids in the critically-ill patient are related to a systemic inflammatory response and increased lipid peroxidation. Clin. Nutr., 22(5): 459-62.
Rasim M, Abdulkerim KB, Esma O, Leyla A, Isik T (2005). Hyperthyroidism causes lipid peroxidation in kidney and testis tissues of rats: Protective role of melatonin. Neuroendocrinol. Lett., 26(6): 806-10.
Russell RM (2004). The enigma of beta-carotene in carcinogenesis: What can be learned from animal studies. J. Nutr., 134 (1): 262 S- 68 S.
Sarandol E, Tas S (2005). Oxidative stress and serum paraoxonase activity in experimental hypothyroidism: Effect of vitamin E supplementation. Cell Biochem. Funct., 23(1): 1–8.
Sato A, Shirota T, Shinoda T, Komiya I, Aizawa T, Takemura Y, Yamada T (1995). Hyperuricemia in patients with hyperthyroidism due to Graves disease. Metabolism, 44: 207-11.
Sawant BU, Nadkarni GD, Thakare UR, Joseph LJ, Rajan MG (2003). Changes in lipid peroxidation and free radical scavengers in kidney of hypothyroid and hyperthyroid rats. Indian J. Exp. Biol., 41: 1334-37.
Shaheen AA, Abdelfattah AA, Siefelvasr M (1996). Influence of verapramil on the efficacy of vitamin E in preventing the ischaemia-reperfusion induced biochemical derangement in cerebral cortex of rat. Drug Res., 47: 670-73.
Solati SM, Attaei L, Azizi F (2007). Lipid oxidation, antioxidants and paraoxonase enzyme activity in patients with subclinical thyrotoxicosis. Ghudad –I Darunriz Va Mitabulim –Iran, 8(4): 317-23.
Stahl W, Sies H (1997). Antioxidant Defense: Vitamins E and C and Carotenoids. Diabetes, 46(Suppl.2): S14-S18.
Stockigt J (2003). Assessement of thyroid function: towards an integrated laboratory-clinical approach. Clin. Biochem. Rev., 24(4): 109-22.
Umesh C, Shobhita C (1999). The Status of Retinoid in Women Suffering from Hyper- andnHypothyroidism: Interrelationship between vitamin A, β-carotene and Thyroid Hormones. Int. J. Vit. Nutr. Res., 69(2): 132-35.
Vrca VB, Skreb F, Cepelak I, Mayer L (2004). Supplementation with antioxidants in the treatment of Graves' disease: the effect on the extracellular antioxidative parameters. Acta Pharm., 54: 79-89.
Weber P, Bendich A, Schalch W (1996). Vitamin C and human health are view of recent data relevant to human requirements. Int. J. Nutr.

Res., 66: 19-30.
Willcox JK, Ash SL, Catignani GL (2004). Antioxidants and prevention of chronic disease. Crit. Rev. Food Sci. Nutr., 44: 275-295.
Wolf G (2002). The regulation of the thyroid-stimulating hormone of the anterior pituitary gland by thyroid hormone and by 9-cis-retinoic acid. Nutr. Rev., 60: 374-77.
Yilmaz, S, Ozan S, Benzer F, Canatan H (2003). Oxidative damage and antioxidant enzyme activities in experimental hypothyroidism. Cell Biochem. Funct., 21: 325- 30.
Zamora R, Hidalgo FJ, Tappel AL (1991). Comparative antioxidant effectiveness of dietary ft-carotene, vitamin E, selenium and coenzyme Ql0 in rat erythrocytes and plasma. J. Nutr., 121: 50-56.

## APPENDIX

### Ethical Committee approval

بسم الله الرحمن الرحيم

جمهورية العراق

وزارة التعليم العالي والبحث العلمي

الجامعة المستنصرية

كلية العلوم

MINISTRY OF HIGHER EDUCATION
& SCIENTIFIC RESEARCH
AL-MUSTANSIRIYA UNIVERSITY
COLLEGE OF SCIENCE

العدد:

التاريخ / /

No .: 136

Date: 24/5/2011

**Ethical committee approval**

**Dear Ese Asoro**

**We are the ethical committee of the chemistry department, college of science, Al-Mustansiriya University. We have studied the project of the M.Sc. student Abass K. Al-Musawi entitle " An Evaluation of Antioxidants and Oxidative Stress in Iraqi Patients with Thyroid Gland Dysfunction" under supervision of Dr. Salwa H.N. Al-Rubae'i and we approval the execution of the project on 20/5/2007 and the student Abass was finished his work and discussed his thesis on 25/6/2009 and have an excellent degree on the thesis. All above documents are in Arabic language if you want as to send them. We provided Dr. Salwa H.N. Al-Rubae'i by this ethical approval because she has desiring to published the paper in African Journal of Biochemistry Research.**

**Professor**
**Dr.Redha I. H. Al-Bayati**
**24/5/2011**

Al-Mustansiriya University
College of Science
Dean Office

**Assistant Professor**
**Dr. Ramzie R. Al-Ani**
**24 /5/2011**

**Assistant Professor**
**Dr. Hussein I. Abdallah**
**24/5/2011**

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