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RESEARCH ARTICLE

The association between serum paraoxonase-1 activity, thyroid hormones and lipids profile in patients with primary hyperthyroidism

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Abstract

Introduction: Changes in serum lipid concentrations occur frequently in disorders of thyroid function. Antioxidant effects of paraoxonase, a high density lipoprotein -associated enzyme that inhibits low- density lipoprotein cholesterol (LDL-C) oxidation in human serum, have been reported. Patients with thyroid dysfunction are more susceptible to oxidative stress, and may show enhanced LDL-C oxidation. **Aim of work:** To find out possible relationship between thyroid hormones, lipids profile levels and serum paraoxonase-1 (PON-1) activity in patients with hyperthyroidism. **Materials and Methods:** The study included 35 hyperthyroid patients (group A) and 35 healthy subjects served as control group (group B). All subjects were subjected to thorough history and clinical examination, laboratory investigations including: thyroid stimulating hormone (TSH), free triiodothyronine (free T3), free thyroxine (free T4), liver and kidney function tests, complete blood picture, fasting and 2 hours post prandial blood glucose, chest X-ray and Doppler ultrasound of thyroid gland. In addition to measurement of total cholesterol (total-C), high-density lipoprotein cholesterol (HDL-C), (LDL-C), triglyceride (TG) and serum PON-1 activity. **Results**: Serum PON-1 activity, TSH, total-C and LDL-C values were significantly low in hyperthyroid patients compared to controls. Serum PON-1 activity was significantly negatively correlated with free T3 and free T4 levels and significantly positively correlated with total-C and TSH levels in hyperthyroid patients. Free T3 and free T4 were significantly negatively correlated with total-C, LDL-C and HDL-C levels, and significantly positively correlated with triglycerides while ,TSH levels were significantly positively correlated with total-C, LDL-C and HDL-C levels and significantly negatively correlated with triglycerides in hyperthyroid patients. **Conclusion:** In hyperthyroidism, PON-1 activity decreased, which is known as an important antioxidant enzyme with cardioprotective effects by protecting LDL and HDL from oxidation. So, this may be associated with increased cardiovascular risk of coronary heart disease in those subjects.
Keywords: Paraoxonase-1 activity, oxidative stress, hyperthyroidism, lipids profile levels

Introduction

The thyroid is one of the largest endocrine glands of the body. Thyroxine (T4) and triiodothyronine (T3), together referred to as thyroid metabolic hormones, play an important role in basal metabolism and the functioning of almost all tissues and systems in the body. In addition to T4 and T3, thyroid stimulating hormone (TSH) secretion

typically is maintained within relatively narrow limits via a sensitive negative feedback loop in which TSH stimulates the synthesis and release of thyroid hormones, that in turn negatively feedback to the hypothalamus and anterior pituitary to limit further TSH release [(1)].

In humans 100% of circulating T4 is secreted by the thyroid gland, but only 20% of T3 is derived from this source. The remaining 80% of T3 is generated by peripheral conversion of T4 to T3 [(2)].

Thyroid hormones are the most important factors involved in the regulation of the basal metabolic condition [(3)]. In addition, thyroid hormones are associated to the oxidative and antioxidative status of the organism [(4)].

Thyroid hormones play a crucial role in biology, acting on gene transcription and the synthesis and degradation of proteins, regulating the basal metabolic rate and mitochondrial oxidative metabolism, and inducing changes in the antioxidant defense system [(5)].

In excessive production of thyroid hormones, the basal metabolic rate can be increased by 100% [(6)].Hyperthyroidism induces a hyperdynamic cardiovascular state that is associated with tachycardia, systolic hypertension, atrial fibrillation, and increased cardiovascular mortality [(7)].

Thyroid hormones influence lipid metabolism, including synthesis, mobilization, and degradation [(8)].

It is well known that alterations in the thyroid function can result in changes in the composition and in the transport of lipoproteins. Specifically, the thyroid hormone stimulates the hepatic de novo cholesterol synthesis by inducing the 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) reductase that catalyzes the conversion of HMG-CoA to Mevalonate, which is the first step in the biosynthesis of cholesterol. Additionally, thyroid hormones activate the low-density lipoprotein (LDL) receptors. The promoter of the LDL receptor gene contains a thyroid hormone responsive element (TRE) which allows T3 to upregulate the gene expression of the LDL receptor. Moreover, thyroid hormones stimulate the cholesteryl ester transfer protein (CETP), an enzyme which transports cholesteryl esters from high- density lipoprotein 2 (HDL2) to the very low density lipoproteins (VLDL) and triglycerides (TG) in the opposite direction. Finally, thyroid hormones stimulate the lipoprotein lipase (LPL) which catabolizes the triglyceride-rich lipoproteins and the hepatic lipase (HL), which hydrolyzes HDL2 to HDL3 [(9)].

Hyperthyroidism triggers lipolysis in subcutaneous tissue, increasing interstitial glycerol levels, lipid oxidation, and circulating fatty acid concentrations [(10)].

It is well known that oxidative stress (OS), defined as an imbalance between radicals and antioxidant defense, is implicated as a pathophysiological mechanism of different diseases and is a topic of growing interest [(11)].

Cell injury is a consequence of OS; recognized targets are DNA, lipids and proteins, which react with hydroxyl radicals to form specific products [(12)].

Antioxidant defenses include enzymatic and non-enzymatic molecules and they are modulated by hormones, which regulate their synthesis and turnover [(13)].

Paraoxonase-1 (PON-1) is an antioxidant enzyme on HDLs that hydrolyzes lipid peroxides in oxidized lipoproteins. PON-1 activity has been suggested to be inversely associated with oxidative stress in serum and macrophages [(14)].

There are three known genotypic forms of paraoxonases. They are coded by the PON set of genes as PON-1, PON-2 and PON-3, located on the long arm of chromosome-7. The differences between them lie in their location and activity. PON-1 is synthesized in the liver and transported along with HDLs in the plasma. It functions as an antioxidant [(15)].

PON-1 is a calcium ion dependent esterase which hydrolyses variety of organophosphorus compounds. In the blood PON-1 is closely attached to HDL particles by apolipoprotein A1. PON-1 inhibits oxidation of low density lipoproteins and also hydrolysis lipid peroxidation products. This enzyme is also involved in decreasing superoxide ion formation. Thus, it is an important antioxidant enzyme. Its serum concentration is influenced by inflammatory changes and the levels of serum oxidized low density lipoproteins [(16)].

PON-1 can exert a protective effect on HDL by preventing it from lipid peroxidation [(17)]. In addition, it has been reported that PON-1 activity is decreased in some diseases due to reactive oxygen species (ROS) pathogenesis under oxidative stress, such as asthma in children or iron deficiency anemia during pregnancy [(18)].

There have been increasing experimental and clinical studies that show the role of free radicals in the etiology of many diseases, and there are increasing data supporting the theory that thyroid disease is associated with increased cardiovascular risk. There have been limited studies about PON-1 levels in hyperthyroidism [(19)].

The present study was designed to investigate the relationship among the serum PON-1 activity, lipid levels, and thyroid hormone status in patients with hyperthyroidism.

Subjects and methods:

This study was carried out on 70 subjects randomly recruited from those attending the endocrinal outpatients' clinic of the department of internal medical, Faculty of Medicine, Zagazig University hospitals. Our study was observational, cross sectional, analytic, case control study, in a period of 6 months during 2014.

Subjects: The included subjects in this study were divided into three groups:

(1) Patients with primary hyperthyroidism (Group A): It included 35 known patients with primary hyperthyroidism (11 men, 24 women), with a mean age of 38.7± 12.3years. The main causes of hyperthyroidism were Graves disease (24 patients), toxic nodular goiter (9 patients), and toxic adenoma (2 patient).

The diagnosis of hyperthyroidism was made on the basis of clinical examination, laboratory investigations (elevated circulating levels of free T4or free T3 and suppressed TSH levels) and ultrasound findings.

(2) Control group (Group B): This group comprised 35 healthy subjects, (14 men, 21 women), matched for sex and age.

Exclusion criteria: Hypertensive patients, diabetics, pregnant, smokers, obese, alcoholic, those on lipid-lowering drugs, antioxidant, vitamin supplements, acetylsalicylic acid, antihistamines, exposure to high-iodine condition , hormone replacement therapy , contraceptive medications, patients with renal and liver diseases , acute, chronic, or malignant diseases were excluded from the study, because these factors may affect the plasma lipid levels and PON-1 activity .

Ethical Clearance: Informed written consents from the patients to participate in the study were taken.

Methods:

All patients were submitted to:

1-Full clinical assessment including history taking, clinical examination, examination for signs of hyperthyroidism and neck examination to detect presence of goiter or nodules.

2-Routine laboratory investigations including:

- Complete blood count.
- Fasting and 2 hours post prandial blood glucose.
- Liver function tests.
- Kidney function tests.

3-Imaging:

- Chest X-ray.
- Doppler ultrasound of thyroid gland.

4-Specific investigations

- Lipid profile including: total-C, TG, LDL and HDL were determined by standard laboratory techniques using enzymatic kits [(20)].
- **Assay of thyroid hormone:** TSH, free T4 and free T3 are estimated by electro-chemiluminescence assay using cobase 411 auto analyzer (Roche diagnostics).
- Assay of serum PON-1 activity: using paraoxon (O, O-diethyl-O-p-nitrophenyl phosphate) [(21)].

Statistical analysis:

Statistical analysis was performed using statistical package for social science (SPSS) version 13. Quantitative data are presented as means ± SD. Qualitative data are presented as number and percentage. The unpaired t-test was used for comparison of means of the continuous variables to evaluate differences between the two groups. Pearson´s correlation was used for detection of relation between 2 variables. P-value>0.05 indicates non- significant results. P-value<0.05 indicates significant results.

Results:

Table (I): Comparison of mean ±SD of different parameters of the study in patients with hyperthyroidism and healthy controls: There was no statistically significant difference of age distribution between the control and patient groups. Free T3 and free T4 levels were significantly higher in the patient group compared to the control group. TSH, total-C, LDL-C values were found to be significantly decreased in hyperthyroidism than controls. TG and HDL-C levels were lower in hyperthyroid patients, but not significantly different between the 2 groups.

Glucose levels were found to be significantly higher in the patient group. Serum PON-1 activity was found to be significantly lower in patients compared to controls.

Table (II): Correlation between Serum PON-1 activity and several parameters of the study in patients with hyperthyroidism (Group A): Serum PON-1 activity was found to be significantly negatively correlated with free T3 and free T4 levels and significantly positively correlated with total-C and TSH levels .

Table (III): Correlation between Serum Free T3, Free T4, TSH and several lipid parameters of the study in patients with hyperthyroidism (Group A): Free T3 and free T4 were found to be significantly negatively correlated with total- C , LDL-C and HDL-C, and significantly positively correlated with TG. TSH levels were found to be significantly positively correlated with total-C levels, LDL-C and HDL-C, and significantly negatively correlated with TG.

Table (I): Comparison of mean ±SD of different parameters of the study in patients with hyperthyroidism and healthy controls.

Parameters	Patients with hyperthyroidism (Group A) (n=35)	Control group (Group B) (n=35)	p
Age (years)	38.7± 12.3	42.3 ± 11.2	NS
Free T3 (pmol/L) (Normal range: 3.1-6.8)	15.6±4.3	3.34±0.4	**<0.0001***
Free T4 (pmol/L) (Normal range: 12-22)	39.35±8.23	14.12±1.5	**<0.0001***
TSH (µU/mL) (Normal range: 0.27-4.2)	0.04±0.03	1.3±0.5	**<0.0001***
TG (mg/dL) (Normal range: <150)	130.2 ± 18.5	138.35 ± 36.6	NS
Total-C (mg/dL) (Normal range: <200)	170.15 ±13.2	202.3±14.3	**<0.0001***
HDL-C (mg/dL) (Normal range: <40)	46.37 ±9.6	49.35 ±5.18	NS
LDL-C (mg/dL) (Normal range: <130)	78.17± 13.43	110.8 ± 9.7	**<0.0001***
Glucose (mg/dL) (Normal range: 70–110)	103.84 ± 15.3	78.6 ± 15.4	**<0.0001***
PON 1 activity (U/ml)	166.42±60.13	237.35±72.24	**<0.0001***

***= P is significant**

TSH= thyroid stimulating hormone**, free T3=** free triiodothyronine**, free T4=** free thyroxine, **TG=** triglyceride, **total-C=** total cholesterol**, HDL-C=** high-density lipoprotein cholesterol**, LDL-C=** low-density lipoprotein cholesterol**, PON-1=** paraoxonase-1

Table (II): Correlation between Serum PON-1 activity and several parameters of the study in patients with hyperthyroidism (Group A).

Variables	PON-1 activity Group A (n=35)	
	r	P
Free T3 (pmol/L)	-0.451	**P < 0.05 ***
Free T4 (pmol/L)	-0.493	**P < 0.05 ***
TSH (µU/mL)	0.562	**P < 0.001***
TG (mg/dL)	0.209	NS
Total-C (mg/dL)	0.395	**P < 0.05 ***
HDL-C (mg/dL)	0.252	NS
LDL-C(mg/dL)	0.189	NS
Glucose (mg/dL)	0.235	NS

***= P is significant**

Table (III): Correlation between Serum Free T3, Free T4, TSH and several lipid parameters of the study in patients with hyperthyroidism (Group A).

	Group A (n=35)					
Variables	**Free T3 (pmol/L)**		**Free T4 (pmol/L)**		**TSH (µU/mL)**	
	r	**P**	**r**	**P**	**r**	**P**
Total-C (mg/dL)	-0.634	**P<0.001***	-0.464	**P<0.05***	+0.505	**P<0.05***
TG (mg/dL)	+0.428	**P<0.05***	+0.599	**P<0.001***	-0.639	**P<0.001***
HDL-C (mg/dL)	-0.465	**P<0.05***	-0.347	**P<0.05***	+0.459	**P<0.05***
LDL-C (mg/dL)	-0.578	**P<.001***	-0.481	**P<0.05***	+0.416	**P<0.05***

***= P is significant**

Discussion:

Thyroid function regulates a wide array of metabolic parameters. Thyroid function significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors [(22)]

Thyroid hormones play a crucial role in the regulation of antioxidants and accelerate free radical production in the mitochondria [(23)]**.** Studies have also shown that thyroid hormones appear to exert a prooxidant activity in target cells [(24)]**.** It has been reported that hyperthyroidism is associated with increased oxidative stress and oxidative damage to lipids and genomic DNA in the aortic wall [(25)]**.**

In our study, both the thyroid hormones T3 and T4 also significantly increased in hyperthyroidism. And TSH was found to be significantly lower in the patients than the controls.

Hyperthyroidism is characterized by reduced serum TSH levels despite increased T4 and T3 levels.

Our finding revealed that, total-C and LDL-C values were found to be significantly lower in the patients than the controls. While TG and HDL-C levels were lower in hyperthyroid patients than controls but without significant difference.

Our results are consistent with a number of studies that have reported the decrease of TG, total-C, LDL-C and HDL-C in hyperthyroid patients than control group [19] [26].

Our study agrees with studies conducted by **Altahir et al., Rizos et al.,** and **Nouh, et al.** They found that hyperthyroidism is associated with decrease the level of total-C, HDL-C, LDL-C and TGs [27] [28] [29].

Thyroid hormones regulate the expression of enzymes in the lipid metabolism [28]. **Kim et al.,** found that, total cholesterol, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol and triacylglycerol levels were found to be decreased in hyperthyroidism and this may be due to the rapid clearing of chylomicron remnants from blood stimulating cholesteryl ester transfer which in turn stimulate lipoprotein lipase. The main cause of the differences in total cholesterol concentrations is the alterations of LDL-cholesterol levels due to the increase in low density lipoproteins receptor mRNA gene expression, which leads to an increase in activity and number of low density lipoproteins receptors and enhance low density lipoproteins receptor-mediated catabolism of low density lipoproteins particles. This in turn, leads to a decrease in concentrations of LDL-C and total-C levels [30].

In hyperthyroid a decrease in HDL-C levels is also observed. This decrease suggested being due to due to increased cholesteryl ester transfer protein mediated transfer of cholesteryl esters from HDL to VLDL and increased hepatic lipase mediated catabolism of HDL2, or due to increased hepatic triglyceride lipase activity [31].

Through the effects of thyroid hormones, hepatic lipase, a decrease in HDL2/ HDL3 is reported. The most prominent alteration in HDL-cholesterol is due to the changes in HDL2 subfraction [32].

Increased LDL-C levels are associated with high CVD risk. We found decreased levels of LDL-C, which were similar to the findings of other studies [8]. Interestingly in hyperthyroidism, LDL-C is reduced, but the risks of several cardiovascular conditions, such as atrial fibrillation, angina pectoris, tachycardia, systolic hypertension, and palpitations, are increased [33]. A hypermetabolic state in hyperthyroidism may be responsible for these conditions.

Thyroid hormones can increase mitochondrial biogenesis, fatty acid oxidation, and tricarboxylic acid cycle activity [34]. Thyroid hormones also have a large impact on glucose metabolism, and novel findings support that hyperthyroidism is associated with insulin resistance [35].

We found significantly higher glucose levels in the patient group compared to the controls, which may be explained by increased endogenous glucose production through more rapid glycogenolysis and gluconeogenesis.

Thyroid hormones have a significant effect on glucose metabolism and the development of insulin resistance. In hyperthyroidism, impaired glucose tolerance may be the result of mainly hepatic insulin resistance [36].

Maratou et al., found that, gluconeogenesis is increased and glycogen synthesis decreased in subclinical and overt hyperthyroidism, as compared to euthyroidism [37].

Serum PON-1 is thought to protect lipoproteins against oxidative modification and is accepted as a preatherosclerotic marker [38]. It has crucial roles in protecting LDL against oxidation and detoxification of highly toxic substances [39].

In our research, we found the PON-1 activity significantly decreased in the hyperthyroid patients as compared to controls.

Aviram et al., found that PON-1reduced oxidized lipids in atherosclerotic lesions that were sampled from a coronary artery or carotid [40]. It has been reported that hyperthyroidism is associated with a higher risk for ischemic stroke among young adults [41]. **Azizi et al.,** showed that a significant reduction in PON-1 activity was observed in both hyper- and hypothyroid patients [42]. **Raiszadeh et al.,** reported that reduced PON-1 activity in patients with hyperthyroidism reverts to normal after euthyroidism [43].

Our study results are in accordance with previous studies showing that PON-1 activity is decreased in hyperthyroidism [43] [44].

Increased production of free oxygen radicals in hyperthyroidism may be responsible for that decrease, or the decreased PON-1 activity may occur as part of an inflammatory response [19].

In hyperthyroidism, an increase in synthesis and degradation of lipids occurs, with a pre-dominance of degradation. Therefore, plasma levels of lipids are reduced in hyperthyroidism [45]. Although this finding can be partly attributed to malnutrition and weight loss, the high uptake of cholesterol into cells and its larger excretion in bile salts through the gut can all contribute to the hypolipemic effect [46]. HDL, especially HDL2 sub-fraction is reduced in hyperthyroidism [47]. Mild hypertriglyceridemia has been paradoxically observed in hyperthyroidism due to direct stimulation of hepatic lipogenesis by thyroid hormones [48].

In our study, serum PON-1 activity was found to be negatively correlated with free T3 and free T4 levels and positively correlated with total-C and TSH levels.

Yavuz et al., reported that PON-1 activity was negatively correlated with serum TT4 and TT3 levels and positively correlated with insulin sensitivity [49]. **Başkol et al.,** also found that, serum PON-1 activity was negatively correlated with free T4 levels and positively correlated with total cholesterol and TSH levels**.** The increase of free T4 levels in hyperthyroidism may cause a decrease in PON-1 activity, which is known as an important antioxidant enzyme with cardioprotective effects [19].

In our study we found that, free T3 and free T4 were found to be negatively correlated with total-C, LDL-C and HDL-C, and positively correlated with triglycerides. TSH levels were found to be positively correlated with total-C , LDL-C and HDL-C, and negatively correlated with triglycerides.

These results were in agreement with that obtained by **Altahir et al., [27].** With respect to lipid metabolism it is clear that the breakdown of TG stored in adipose tissue is enhanced by thyroid hormones excess, resulting in concentration and turnover of non-esterified fatty acids (NEFA) **[50].** This increased availability of fatty acids is associated with a rise in the lipid oxidation rate **[51].**

Hyperthyroid patients have also low plasma cholesterol levels may be due to an increased biliary excretion of cholesterol. It has been hypothesized that the low plasma cholesterol level of hyperthyroidism patients may be due to an increased clearance rate **[52].**

T3 up regulates LDL receptors by controlling the LDL receptor gene activation. This T3 mediated gene activation is done by the direct binding of T3 to specific thyroid hormone responsive elements (TREs). Furthermore, T3 controls the sterol regulatory element-binding protein-2 (SREBP-2), which in turn regulates LDL receptor's gene expression. T3 has also been associated with protecting LDL from oxidation. Another effect of T3 is the up-regulation of apolipoprotein AV (ApoA-V), which plays a major role in TG regulation. Indeed, increased levels of ApoA-V have been associated with decreased levels of TGs. Proposed mechanisms for this effect include the decrease of hepatic VLDL-TG production and the increase of plasma LPL levels and activity, resulting in increase of lipoprotein remnant generation due to enhanced LPL-mediated lipolysis of VLDL-TG . Moreover, a greater clearance of lipoprotein core remnants, caused by increased hepatic up-take due to an enhanced affinity for the LDL receptor, has also been ascribed to ApoA-V **[28].** The elevation of TGs in hypothyroidism is caused by a reduced removal rate of TG from plasma due to a decrease in the activity of hepatic TG lipase **[53].**

Thyroid hormones influence all aspects of lipid metabolism including synthesis, mobilization, and degradation **[8].** Thyroid hormones stimulate cholesterol synthesis by inducing HMG-CoA reductase in the liver **[48].** Thyroid hormones affect lipoprotein lipase activity and thus, the hydrolysis of triglycerides into VLDL and chylomicrons into fatty acids and glycerol **[8].**

In hyperthyroidism, although lipoprotein lipase activity is usually normal**[54],**an increased liver fatty acid synthesis and oxidation is observed due to enhanced acetyl-CoA carboxylase 1 and carnitine palmitoyl transferase Ia expression leading to increased VLDL biosynthesis **[55].**

Thyroid hormones affect cholesteryl ester transfer protein and hepatic lipase activity, which are increased in hyperthyroidism and decreased in hypothyroidism, with consequent changes not only in total -HDL but also in HDL subfraction levels [56].

Furthermore, thyroid hormones, by binding to the thyroid hormone receptor, inhibit through a competitive action the liver X-receptor-mediated ATP-binding cassette transporter A1 gene expression, resulting in decreased HDL levels in patients with hyperthyroidism and increased in hypothyroidism **[55].** Experimental evidence suggests that thyroid hormones might also affect cholesterol-7alpha-hydroxylase in liver [57].

Thyroid hormones, especially T3, induce LDL receptor gene expression in the liver, enhancing LDL clearance and explaining the decreased or increased LDL levels observed in hyperthyroidism and hypothyroidism, respectively **[8].** Thyroid receptors seem to mediate the effects of thyroid hormones on lipid metabolism, and more specifically alpha 1 receptors control the lipogenesis in white adipose tissue, and β receptors regulate the activity of lipogenic and lipolytic enzymes in the liver **[8] [55].**

Study of **Xu et al.,** have confirmed the presence of an inverse relationship between serum thyroxin and cholesterol levels. Interestingly, in vivo and in vitro research on the function of TSH has shown that TSH, independent of thyroid hormones, can upregulate the expression of hepatic HMG-CoA reductase , which is the rate-limiting enzyme in cholesterol synthesis, and increase the cholesterol content in the liver . Therefore, we hypothesized that TSH, independent of thyroid hormones, would be positively associated with the serum cholesterol level **[58].**

Reverse cholesterol transport can also involve the transfer of cholesterol esters from HDLs to VLDLs and LDLs. This transfer requires the activity of the plasma glycoprotein CETP. The transfer of cholesteryl esters from HDLs to VLDLs via CETP activity also involves an exchange of triglycerides from the VLDLs to the HDLs. VLDLs are eventually converted to LDLs and the cholesterol acquired from HDLs can be returned to the liver via the

interaction of LDL with the hepatic LDL receptor. HDL-C levels also tend to decrease because levothyroxine stimulates the CETP [59].

In conclusion, in hyperthyroidism, PON-1 activity decreased, which is known as an important antioxidant enzyme with cardioprotective effects by protecting LDL and HDL from oxidation. So, this may be associated with increased cardiovascular risk of coronary heart disease in those subjects.

Recommendations:

It is important to achieve an euthyroid state as possible in hyperthyroid patients. Effective antioxidant therapy to increase PON-1 activity may be a therapeutic option in patients with hyperthyroidism. Also, further study on a large number of patients to support the role of PON-1 activity in the follow up and prognosis of hyperthyroidism.

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