International Journal of Pharmaceutical and Bio-Medical Science

ISSN(print): 2767-827X, ISSN(online): 2767-830X

Volume 03 Issue 10 October 2023

Page No: 557-567

DOI: https://doi.org/10.47191/ijpbms/v3-i10-10, Impact Factor: 6.858

Correlation of Selenium Level, Malondialdehyde (MDA) and Total antioxidant Status (TAS), with Thyroid Hormones in Hypothyroidism Women

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ABSTRACT

Background and objective: The thyroid gland and its hormones are crucial for the development of the body's organs as well as the balanced regulation of the body's fundamental physiological processes and . One of the most prevalent thyroid conditions in adults is hypothyroidism, often known as myxedema. The study's objective was to discover thyroid hormones in women with hypothyroidism, including selenium levels, malondialdehyde (MDA), and total antioxidant status (TAS), since these indicators may suggest thyroid health.

Materials and Methods: In this case-control research, which comprised 70 hypothyroid women and 30 controls who appeared to be in good health, the participants' ages varied from 20 to over 40. People who attended the laboratory at Imam Al-Sadiq Hospital and Merjan General Hospital were selected as hypothyroid patients.The serum concentrations Selenium Levels, Malondialdehyde (MDA) and Total antioxidant Status (TAS), total triiodothyronine (T3), total thyroxin (T4), thyroid stimulating hormones (TSH), were measured in 100 samples, mini-vidas were employed for T3,T4,TSH measurment. while Electrofluorescence immunoassay was used to measure the , Malondialdehyde (MDA) and Total antioxidant Status (TAS), levels Selenium and concentration**. Results** : TSH levels 22.73 nmol/L were significantly higher ($P < 0.05$) in hypothyroid patients compared to controls 1.77 nmol/L, while levels of T3 1.41 nmol/L and T4 55.22 nmol/L were significantly lower ($P < 0.05$). In hypothyroid patients compared with the control group 2.08 nmol/L, 81.81 nmol/L respectively while malondialdehyde (MDA) levels were 35.16±2.2 (ng/ml) Significantly higher ≤0.0001) in women with hypothyroidism and total antioxidant status (TAO) 175.07±3.8 (mg AAAE/ml) There was a significant reduction in Total antioxidant status as well as selenium concentration was 12.14±0.9 (ng/ml) ($P < 0.011$) among women with hypothyroidism and healthy women, respectively.

Conclusion: People with hypothyroidism who are potentially at risk for thyroid problems may be better detected in women who have lower selenium levels and total antioxidant status with significantly higher malondialdehyde (MDA) levels

KEYWORDS: Selenium, Malondialdehyde (MDA) ,Total antioxidant Status (TAO), Hypothyroidism, T3,T4, and TSH.

ARTICLE DETAILS

Published On:
26 October 2023

Available on:
https://ijpbms.com/

INTRODUCTION

The most prevalent thyroid gland condition is hypothyroidism, also known as myxedema in adults and cretinism in children. Depending on the cause of the insufficiency, hypothyroidism can be primary or secondary. More than 99.5% of instances of hypothyroidism (also known as primary hypothyroidism) are caused by hypofunction of the thyroid gland, with the remaining 0.5% of cases being caused by pituitary and hypothalamus malfunction. (Luo et al., 2021). An often overlooked thyroid condition, hypothyroidism is the most common. Compared to men, women suffer 5–10 times more (Vanderpump et al ,. 2002).

An estimated 13 million Americans have hypothyroidism but lack a diagnosis (Helfand, 2004).The symptoms of hypothyroidism include tiredness, slurred speech, and memory loss. Menstruation, ovulation, and fertility are all impacted by thyroid hormone ((Shahid et al., 2018). Reactive oxygen species (ROS), which are essential, are required during the initial stages of thyroid hormone production, which take place during iodide oxidation. The thyroid hormones' management of mitochondrial function controls metabolism as well. Since ROS are necessary for the thyroid to function, the organ is particularly susceptible to oxidative damage .(Benvenga et al., 2021).In addition to H2O2-dependent biosynthesis and the (in-)activation of thyroid hormones, which is necessary for their receptor-mediated cellular action, selenocysteine-containing proteins also offer cellular defense. Unbalances between the thyroid's selenium levels contribute to common illnesses such as autoimmune thyroid disease and metabolic disorders that are linked to disrupted thyroid hormone status (Köhrle, 2021). Epidemiological research has shown that selenium insufficiency affects a significant portion of people worldwide (Schomburg et al.,2020) Anti-thyroid antibodies are more prevalent in patients with aberrant thyroid profiles. As for the relationship between MDA and thyroid hormones .ROS play a significant role in maintaining healthy thyroid function. Oxidase synthesis from thyroid cells is catalyzed by the release of these enzymes (Dupuy et al., 1991; Ameziane, 2016). Since the thyroid gland depends on ROS to operate, it is especially vulnerable to oxidative injury. As a result, the thyroid's antioxidant defense mechanism must properly control ROS generation and scavenging.(Pace *et al*.,2020)

The most significant variables affecting the basal metabolic rate during physiologically normal states are thyroid hormones, which change the oxygen consumption of mitochondria, the major source of free radical generation. Thus, any changes in thyroid hormone levels may have an impact on the formation of free radicals in the mitochondria. (Oziol *et al.*, 2003). Thyroid peroxidase (TPO)-catalyzed hormone requires dual oxidases (DUOX), enzymes needed for hydrogen peroxide production.(Ohye and M. Sugawara , 2010). Free oxygen radicals are mostly produced in mitochondria, where they can damage organs by oxidizing cellular macromolecules including proteins, lipids, and carbohydrates.

MATERIALS AND METHODS

Subjects

This was a case-control study that has been carried during the period at the beginning of June 2022 until the end of November 2022 under the supervision of specialized doctors. Samples collected from hypothyroidism women with different age groups, varied between 20 to more than 40 years old. study including 70 from hypothyroid women and 30 apparently healthy women as control group who do not have a history of any hypothyroidism, hyperthyroidism, anemia, or family history of metabolic disease.

METHODS

Serum preparation

A totaleof 100 serum samplese were gathered from the Imam Al-Sadiq Hospital's counseling and endocrinology departments. Additionally, external laboratories in the city of Hilla In order to obtain samples for the current study, 5 ml of intravenous blood was drawn through single-use medical syringes and blood was placed in the gel tubes with an airtight lid. The pipes were then placed in a centrifuge for 10 minutes at room temperature, rotating at 3000 rpm, and the serum was extracted. The serum gel tube is divided into several sections in the Eppendorf tube, by microbibet, and stored at -20 degrees. Thyroid hormone levels in the serum are estimated using the manufacture of Biomerieux's mini-vidas. Using a tool of German origin and a group of American company, ELISA technology was used to calculate the levels of of Selenium Levels, Malondialdehyde (MDA) and Total antioxidant Status (TAS). The probability threshold $p < 0.05$ was used to compare kits using the Duncan test in the 26th edition of Statistical Programs (SPSS). By determining the values of the correlation coefficient (R) and the correlation coefficient between the analyzed data, the correlations were studied and the correlation was assessed [12-13].

Ethical approval

The study has been conducted in accordance with the guidelines. Ethical contained in the Helsinki Declaration. Before sampling, verbal and other analytical consent was obtained for the patient. In order to obtain this permission, the study protocol, subject information, approval form and delegation were assessed by the local ethics committee in accordance with document No. 100 (which contains the number Z22120 and approval date: 6-12-2022).

RESULTS

4-1-Distribution of Study Population According to Age

A total of 70 patients with hypothyroid and 30 apparently healthy women were recruited for this study. they were classified into three age groups, the first age group being under 20 years, from 20 to less than 40 years, more than 40 years, consisting of 15(21.43%), 20(28.57%), 35(50%) respectively for hypothyroidism women, and 30 healthy women as control group include 10(33.33%) women for each age as appeared in table-1.

Table 1- Distribution of Samples According to Age Group.

Groups / Age (year)	Hypothyroid women	Healthy women
	No. (%)	
<20	15 (21.43)	10 (33.33)
21-40	20 (28.57)	10 (33.33)
>40	35 (50)	10 (33.33)
Total	70(100)	30 (100)

There were a significant decrease for Thyroxin (T4) 55.22 nm/L, 81.81 nm/L Triiodothyronine(T3) 1.41 nm/L**,** 2.08 nm/L concentrations between hypothyroid women and healthy women respectively, while there was a significant increase for Thyroid Stimulating Hormone(TSH) it was 22.73 nm/L and 1.77 nm/L for hypothyroidism women and healthy women respectively P<0.0001 as shown in table2.

4-2- level of Tri iodothyronine (T3) , Thyroxine (T4), and Thyroid Stimulating Hormone(TSH).

Table 2- Levels for Thyroxin (T4), Tri-Iodothyronine (T3) and Thyroid Stimulating (TSH) Hormones in Hypothyroidism Women and Healthy Women.

Groups / Parameters	Hypothyroidism women	Healthy women	p-value
	Mean ±S.E		
T4 nm/L	55.22±11.5	81.81±4.2	**0.002****
T3 nm/L	1.41±0.1	2.08±0.06	**0.040***
TSH nm/L	22.73±2.7	1.77±0.4	**≤0.0001****

While there were a significant increase for Thyroxin hormone T4 70.48 nm/L at second age group (21-40) in contrast to other age groups within hypothyroid women, while there was a significant decrease for T3 1.32 nm/L at <20 years old age group and a significant decrease for TSH 19.7 nm/L for second age group (21-40 years old) as appeared in table 3

Table 3- Levels for Thyroxin (T4), Tri-Iodothyronine (T3) and Thyroid Stimulating (TSH) Hormones in Hypothyroidism Women According to Different Age Groups.

Parameters	<20	21-40	>40
	Mean ± S.E		
T4 nm/L	47.59±6.6 **a**	70.48±1.2 **b**	55.22±6.1 **a**
T3 nm/L	1.32±0.6 **a**	1.63±0.3 **b**	1.72±0.2 **b**
TSH nm/L	24.27±3.6 **b**	19.70±2.8 **a**	24.89±3.8 **b**

a,b - the Differences in Measurements that Carry Different Letters are significant (p<0.05).

Table -4- illuminate comparison between Hypothyroidism women and healthy women according to different age groups. There were a significant decrease for T4 hormone 47.59 nm/L , 55.22 nm/L at first (>20) and third(<40) age groups in contrast to control group 82.30 nm/L, 79.49 nm/L in order. While there were a significant decrease for T3 hormone1.32 nm/L, 1.63 nm/L for first(>20) and second (21-40) age groups in relation to healthy women 2.11 nm/L, 2.01 nm/L respectively. Also there was a significant increase for TSH hormone 24.27 nm/L, 19.70 nm/L, 24.89 nm/L for all age groups in hypothyroidism women in compare with healthy women 2.04 nm/L, 1.23 nm/L, 1.57 nm/L accordingly.

Table 4- Comparing The Levels of Thyroxine (T4), Tri-Iodothyronine (T3) and Thyroid-Stimulating Hormone (TSH) in Hypothyroidism Women to Those in Healthy Women According Age Groups.

Parameters	Age(year) / Groups	>20	21-40	<40
		Mean ± S.E		
T4 nm/L	**Hypothyroidism women**	47.59±6.6	70.48±1.2	55.22±6.1
	Healthy women	82.30±4.4	83.39±7.1	79.49±5.5
p-value		**≤0.0001****	**0.962**	**0.001****

Correlation of Selenium Level, Malondialdehyde (MDA) and Total antioxidant Status (TAS), with Thyroid Hormones in Hypothyroidism Women

T3 nm/L	**Hypothyroidism women**	1.32±0.6	1.63±0.3	1.72±0.2
	Healthy women	2.11±0.9	2.01±0.1	2.15±0.1
p-value		**≤0.0001****	**0.023***	**0. 502**
TSH nm/L	**Hypothyroidism women**	24.27±3.6	19.70±2.8	24.89±3.8
	Healthy women	2.04±1.1	1.23±0.2	1.57±2.7
p-value		**≤0.0001****	**≤0.0001****	**≤0.0001****

The table below showed a significant decrease (P<0.011 *) in selenium concentrations (12.14 ng / ml) for the group of hypothyroid women compared to (19.75 ng / ml) for healthy women. There was a significant increase in Malondialdehyde (MDA) as it was (35.16 mmol/L) for hypothyroid women and (26.92 mmol/L) for healthy women, respectively (P < 0.0001**). As for the total antioxidant status (TAS), it appeared a significant decrease (P<0.026 *) in the group of patients (175.07 mg AAE / ml) compared to (196.25 mg AAE / ml) in the group of healthy women. as seen in table (5).

4-3 : Level of Selenium, Malondialdehyde (MDA) and Total antioxidant Status (TAS) in Hypothyroidism and healthy women .

Table 5- Level of Selenium, Malondialdehyde (MDA) and Total antioxidant Status (TAO) in Hypothyroidism and Healthy Women By age Groups.

Groups / Parameters	**Hypothyroidism women**	**Healthy women**	**p-value**
	Mean±S.E		
Selenium (ng/ml)	12.14±0.9	19.75±1.7	**0.011***
MDA(mmol/l)	35.16±2.2	26.92±2.1	**≤0.0001****
TAO (mgAAE/ml)	175.07±3.8	196.25±5.6	**0.026***

This table shed light on a comparison between a group of hypothyroid women and a group of healthy women by different age groups. Selenium results showed a significant decrease of 10.34 g/mL. 11.09 ng/ml for The first and third age groups in contrast to the healthy group 20.85 ng/ml, 19.21 ng/ml for the group in order. While Malondialdehyde (MDA) it increased significantly in the three age groups in women with hypothyroidism compared to healthy women. As for the antibody, there were no statistically significant differences for the other age groups.

Table -6- Level of Selenium Levels, Malondialdehyde (MDA) and Total antioxidant Status (TAS), in Hypothyroidism and Healthy Women By age Groups.

Parameters	**Age(year) Groups**	**1-20**	**21-40**	**>40**
		Mean±S.E		
Selenium (ng/ml)	Hypothyroidism women	10.34±1.7	13.25±2.7	11.02±0.4
	Healthy women	20.85±2.4	19.20±1.9	19.21±0.2
p-value		**≤0.0001****	**0.056**	**0.014***
MDA(mmol/l)	Hypothyroidism women	35.04±5.1	36.55±4.2	34.01±2.2
	Healthy women	27.77±3.2	28.16±1.8	24.01±1.5
p-value		**0.022***	**0.005****	**≤0.0001****
TAO (mgAAE/ml)	Hypothyroidism women	177.57±11.2	170.75±5.5	174.18±9.4
	Healthy women	197.14±9.8	195.87±3.9	194.71±4.7
p-value		**0.122**	**0.149**	**0.744**

Table-7- Shows the levels of selenium, malondialdehyde (MDA), and total antioxidant status (TAS) in hypothyroidism in women by age group. Which showed a significant difference in the value of selenium in the second age group compared to the first and third groups. As for malondialdehyde (MDA) and total antioxidant status (TAS), there were no significant difference between the three age groups. As appeared also in the following figures (1), (2),(3)

Table -7- Levels of Selenium, Malondialdehyde (MDA) and Total antioxidant Status (TAS) in Hypothyroidism Women By age Groups.

Parameters	1-20	21-40	>40
	Mean±S.E		
Selenium (ng/ml)	10.34±1.7 **a**	13.25±2.7 **b**	11.02±0.4 **a**
MDA (mmol/l)	35.04±5.1 **a**	36.55±4.2 **a**	34.01±2.2 **a**
TAO (mgAAE/ml)	177.57±11.2 **a**	170.75±5.5 **a**	174.18±9.4 **a**

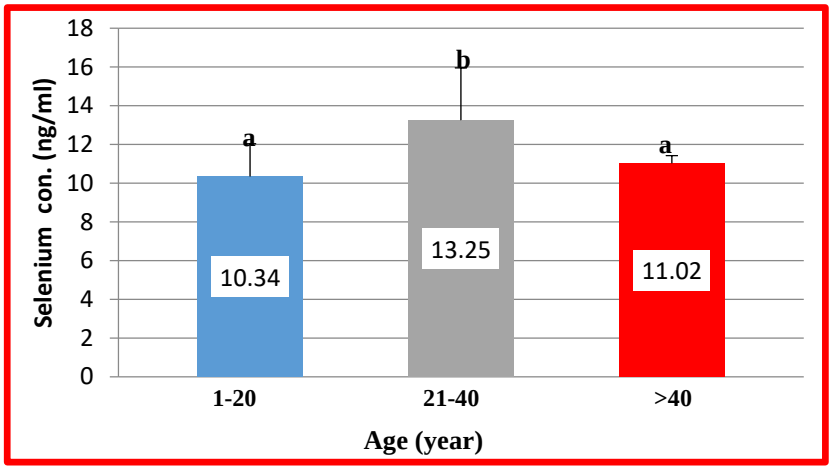


Figure (1) Levels of Selenium in Hypothyroidism Women By age Groups.

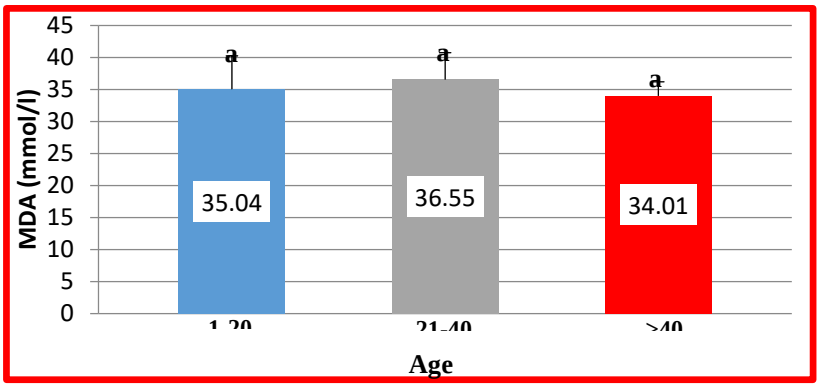
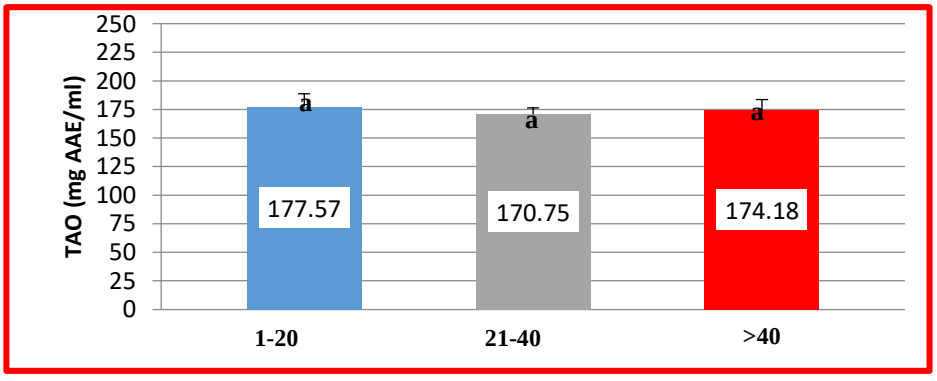


Figure (2)Level of Malondialdehyde (MDA) in Hypothyroidism Women by age Groups.



Age (year)

Figure (3) Level of Total antioxidant Status (TAS) in Hypothyroidism Women by age Groups.

4-4- Correlation Coefficient among all Studied Parameters.

indicates that there is a significant negative relationship for both selenium and anti-TPO levels, as shown in the following figures (1-4), There is a positive relationship between triiodothyronine (T3) and thyroxine (T4), as well as between total antioxidant status (TAS) and thyroid-stimulating hormone (TSH) in hypothyroidism, as shown in the following figures (1-5),(1-6).

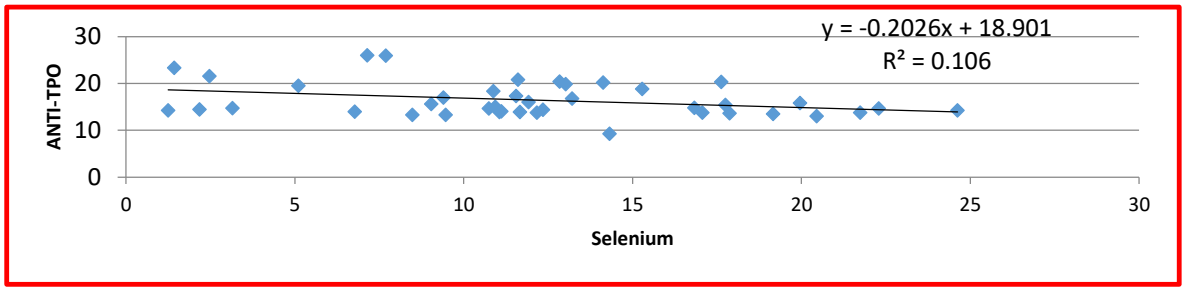


Figure (1-4) negative Significant correlation between selenium and Anti -TPO.

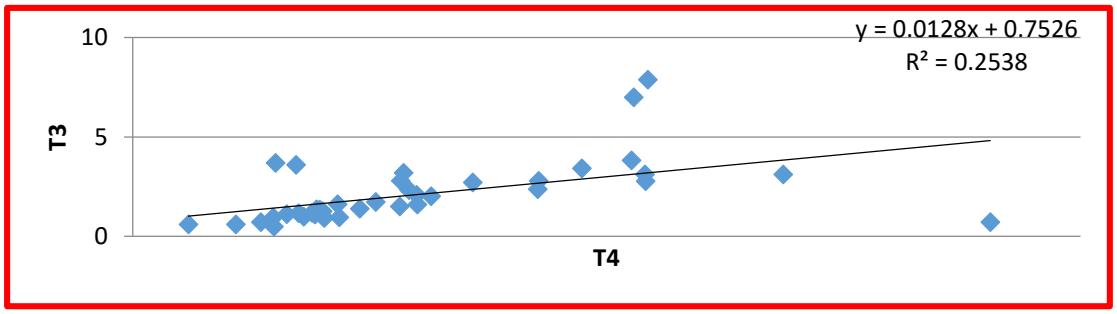


Figure (4-22) Significant correlation between T4 and T3.

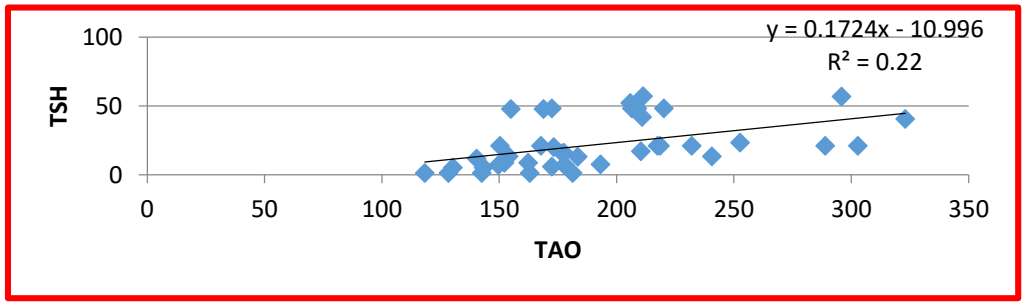


Figure (1-6) positive Significant correlation between Total antioxidant and Thyroid stimulating hormone.

DISCUSSION

In the present case-control study of 70 female patients with thyroiditis and 30 healthy women, serum TSH levels were significantly higher in women with hypothyroidism than in normal subjects, while total T3 levels were And total T4 is at a lower level in women with hypothyroidism compared to the group of healthy women. This came out similar to researchers (Hadlow et al., 2013; Cooper et al., 2018) thyroid-releasing hormone (TSH) stimulates the secretion of thyroid-stimulating hormone (TSH) from the anterior pituitary gland. TSH, in turn, stimulates the thyroid gland to release thyroxine (T4) and triiodothyronine (T3), which are present in a free, active form and a bound, inactive form. A negative feedback mechanism exists between TSH and thyroid hormones (Hadlow et al., 2013; Cooper et al., 2018). As the results of our research showed that the prevalence of the disease increases with age, advanced age and hypothyroidism are linked. The recommended range of TSH also rises with age, with a significant decrease in the secretion of thyroid hormones as a result of the deficiency of elements such as selenium, and others important in the synthesis of anti-tpo, which is involved in the Initial steps of building and formation of the thyroid gland. This is what Leng and his colleagues show from the fact. The population distribution of

TSH concentration increases steadily with age. Recent evidence from observational research suggests that older adults have higher levels of TSH in the blood (Aggarwal et al., 2013; Carlé et al., 2016).

Selenium, a non-metallic element, is a micronutrient essential for the biosynthesis of selenoproteins containing selenocysteine. In adults, the thyroid contains the highest amount of selenium per gram of tissue. Most known selenoproteins, such as glutathione peroxidase, are expressed in the thyroid and are involved in thyroid hormone metabolism, redox state regulation, and maintenance of cellular homeostasis(Dijck-Brouwer *et al.*, 2022). Some clinical studies have shown that lack of selenium will increase the prevalence of several kinds of thyroid diseases (Mao *et al*., 2016; Dijck-Brouwer *et al.*, 2022).

Our results found a significant decrease for selenium concentration in hypothyroidism women compared to non hypothyroidism women that agreed with (Ferrari *et al*., 2021) research.

The thyroid is one of the highest content of Se in the body organs, it is interesting to note that in the case of Se deficiency, the Se content of thyroid gland is also high (Duntas, 2010) research on Patients with Se deficiency can benefit from Se supplementation, while Se supplementation in people with adequate Se levels can exacerbate the risk of certain diseases (Rayman *et al*.,2021).

Se is present in selenoproteins in the form of selenocysteine, which is involved in constituting the active center of selenoproteins. It plays an important role in the metabolism of thyroid hormones and in the fight against oxidative stress (Duntas, 2010) Selenoproteins such as GPXs and TRs can scavenge H2O2, protect cell membrane structure and function, repair the site of molecular damage, achieve antioxidative stress and local protective effects against oxidative stress or inflammation. In Se deficiency, GPx activity decreases, degradation of H2O2 is reduced, thyroid cells are less resistant to oxidative stress, apoptosis and cell death occur (Rotondo Dottore *et al*., 2017). On the other hand, the activity of DIOs is reduced in Se deficiency also is often accompanied by a loss of immune function (Spallholz *et al*.,1990; Taylor ,1995). In cellular immunity, Se may reduce thyroid antibodies by upregulating activated Treg cells (Hu *et al*., 2021). Se deficiency may upregulate Th1/Th2 effectors and enhances immune responses. The possible therapeutic effect of Se in HT to improve immune function was validated in a study conducted in 2022, which showed that Se supplementation with 100ug per day improved thyroid function and the quality of life of patients by decreasing interferon gamma concentrations and increasing interleukin 1b concentrations (Kryczyk-Kozioł *et al*.,2022). Selenium (Se) plays a large role in the functioning of the human organism used in the biosynthesis of selenium proteins (proteins containing one or more selenocysteine residues). The functions of human selenoproteins in vivo are very diverse, Many selenoproteins have antioxidant activity (Minich *at el* ,. 2022).

Through the results we noticed a clear decrease in the concentration of selenium in terms of age and weight for the group of patients compared to the group of healthy women, which may affect deiodinase enzyme responsible for converting T4 to T3 via the needs to selenoprotein.

TPO enzyme responsible for Thyroid peroxidase (TPO) is a unique enzyme localized in the apical membrane of thyroid follicular cells involved in the biosynthesis of thyroid hormone. TPO has two active sites, which facilitate iodinating tyrosine residues in thyroglobulin (Tg) in close conjunction with dual oxidase (DUOX) and H_2O_2 followed by intrachain coupling of two iodotyrosines residues to form thyroid hormone (Stathatos and Daniels, 2012). Selenium is also an antioxidant , GPX needs it to get rid of free radicals resulting from the binding of active iodine to thyroid hormone by the action of TG to form a hormone, and therefore its deficiency leads to a decrease in thyroid hormones, which causes hypothyroidism. This is consistent with the researcher's opinion Minich (2022) Several selenoproteins exhibit an antioxidant effect in the thyroid gland. Selenium is an essential element in the metabolism of thyroid hormones. High concentrations of anti-thyroid antibodies (predominantly anti-TPO (TPOAb) and antithyroglobulin antibodies are present in most patients with autoimmune thyroiditis but also occur in ~10% of the euthyroid general population (Hollowell *et al*.,2002). Another research (Hariharan *et al.,* 2020) showed that glutathione peroxidase (GPX) is a major selenoprotein present in the human body, which helps in controlling the excessive production of free radicals at the site of inflammation.

Regarding thyroid disease Maintaining a physiological concentration of selenium is a prerequisite for preventing thyroid disease and maintaining general health. Selenium intake in particular is associated with autoimmune disorders. This is consistent with researcher Ventura (2017) who showed that maintaining a physiological concentration of selenium is a prerequisite for preventing thyroid disease and maintaining health,also suggests that selenium supplementation for patients with autoimmune thyroiditis is associated with improved quality of life and improved thyroid ultrasound features and is associated with decreased levels of peroxidase antibodies.

Se deficiency is a risk factor for enlarged thyroid gland size, hypothyroidism, and thyroid nodules, and Se supplementation could reasonably be suggested in Se-deficient geographic areas in thyroiditis patients in Hashimoto (HT). For example, Se (100 μg/day for 6 months) significantly reduced the level of thyroid peroxidase antibodies when administered in newly diagnosed, previously untreated HT patients with hypothyroidism or subclinical hypothyroidism living in a Polish region with low Se status (Kryczyk-Kozioł *et al* ,. 2021). the appropriate range of serum

Se is narrow (approximately 90–120 μg/L, estimated according to GPx activity and serum selenoprotein concentration), and below and above this will increase the risk of deficiency and toxicity, with potential adverse effects on Health (Cape *et al*., 2015). Furthermore, administration of 200 μg/day of Se yeast tablets for at least 6 months in HT patients improves thyroid antibodies and thyroid function by increasing antioxidant activity (Hu, Y., *et al* .,2021) .

A study by (Wichman *et al*., 2016) appeared low levels of Se are associated with an increased risk of developing thyroid antibodies, and Se supplementation can reduce TPOAb titers, that Se supplementation reduced thyroid antibody levels after 3, 6, and 12 months in the LT4-treated autoimmunothyroiditis(AIT) group and after 3 months in the untreated AIT group.

While a research by (Ray *et al* ., 2012) illustrate that many selenoproteins exhibit antioxidant properties and can scavenge reactive oxygen species (ROS) formed as by-products of molecular oxygen reactions in the process of oxidative phosphorylation in cells. ROS can also be generated by external agents, such as drugs, xenobiotics, metals, radiation, smoking, and infection .

Ray *et al* ., (2012) indicated in his research Se and selenoproteins play a significant role in the development of thyroid cancer. It is generally agreed that oxidative stress plays an important role in cancer genesis and tumour progression. Most studies indicate an association between Se deficiency and the development of thyroid cancer, as well as significant changes in the expression and activity of various selenoproteins in different types of thyroid cancer.

In this present case-control study, showed significant differences in MDA level for women with hypothyroidism which agreed also Furthermore (Resch *et al*., 2002) found an increase in malondialdehyde (MDA) level in obese hypothyroid women. The synthesis of thyroxine (T4) and triiodothyronine (T3) catalyzed by thyroid peroxidase (TPO) in thyroid follicles is a very complex process involving ROS, notably, H2O2 (Pace *et al.*,2020).

ROS are already essential in the initial stages of thyroid hormone production, during iodide oxidation . Additionally, thyroid hormones perform a metabolic regulatory function by affecting mitochondrial activity (Thanas and Ziros,2020). Because of the reliance on ROS in its function, the thyroid is particularly exposed to oxidative damage, Therefore, the antioxidant defense system of the thyroid must effectively regulate ROS production and scavenging (Szanto *et al.*,2019).

a higher level of MDA in hypothyroid patients Due to the increase in the production of RONS, the resulting aldehyde has cytotoxic, mutagenic and carcinogenic effects. It is expected that this is due to the increase in free radicals that will affect the cell envelope and break it due to the ability of the free electron present on the wall of free radicals that enables it to adhere and react quickly, causing damage to the wall. and destroying the cell, and thus an increase in lipid peroxidation is formed, which rises, as Malondialdehyde is the final product of it.

In a study (Wang *et al.,* 2023) showed that reactive oxygen species (ROS) mediate lipid peroxidation and produce 4-hydroxynonenal and other related products, which play an important role in the process of cell death, including apoptosis, autophagy, can promote lipid peroxidation. Phospholipids mediate mitochondrial apoptosis, endoplasmic reticulum stress, and other complex molecular signaling pathways to regulate apoptosis. Lipid peroxidation and its products also act in different stages of autophagy (Kander *et al.*, 2017).

Chakrabarti and others (2016).found that MDA concentration as a marker of oxidative stress were higher in patients with hypothyroidism prior to levothyroxine treatment and/or selenium supplementation than in the control group. MDA concentration has also been found to decrease after treatment and/or supplementation in patients with hypothyroidism. In addition, they obtained a significant positive association between MDA level and baseline TSH values.

In hypothyroidism, including its subclinical form (Torun *et al* ,.2009) observed elevated levels of MDA, compared to healthy individuals. Apart from insufficient antioxidant defense, this may be related to altered lipid metabolism in thyroid cells which matched to this study.

Accumulation of oxygen free radicals may inhibit TPO activity, consequently interfering with thyroid hormone production and leading to the development of hypothyroidism (Ohye *et al*., 2010) .

Under normal circumstances, epithelial cells of the thyroid have a moderateproduction of reactive oxygen species (ROS)that are physiologically required for theformation of thyroid hormones. These are not necessarily toxic because they are continuously toxicized by the synthesis of the hormone or the endogenous antioxidant system (Mogulkoc *et al*., 2005) .

The findings of the present investigation suggested the existence of several important linkages.

T3 and T4 have a positive significant connection with a value of (P< 504*) in the group of hypothyroid women.

The thyroid-stimulating hormone (TSH), which is connected to aging because it rises with age and with gender since it rises higher in women than in men, is inversely related to this connection.

This was supported by the findings of researcher Rosharga and his team in (2014). who found that a negative feedback mechanism maintains hormonal balance in the body by causing T3 and T4 to fall and TSH to considerably rise.

This study also showed a significant positive relationship (P< 469*) between thyroid-stimulating hormone (TSH) and total antioxidant activity (TAS), which occurs due to TPO deficiency. According to researcher (Bjoro et al.,

2000). TPO deficiency prevents the synthesis of GPX, which in turn prevents the reduction of free radicals (ROS) formed in the form of H2O2 so that they are converted into useful H2O, which is what happens when GPX levels decrease. Free radicals (ROS) rise, and malondialdehyde increases (MDA). Total antioxidants (TAS) decrease.

Selenium and Anti-TPO exhibited a significant (P<326) unfavorable relationship because of the part selenium plays in the synthesis of anti-TPO . This happens when TPO drops or anti-TPO increases as a result of selenium's role in the creation of TPO, which participates in the first two stages of the production of the thyroid hormones T3 and T4. Selenium deficiency leads to TPO deficiency, which inhibits the production of thyroid hormones via idoidonase, an enzyme that promotes the bonding of glutathionine (TG) with iodine.

ACKNOWLEDGMENTS

The authors thank the laboratory staff at Al-Hillah city hospitals (Al-Hillah Teaching, Mergan, and Imam AL-Sadiq Teaching), hospitals (in Iraq for processing clinical specimens to facilitate research requirements .

Conflicts of interest

There are no conflicts of interest.

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