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ORIGINAL PAPER

Oxidative stress and antioxidants markers in individuals with thyroid hormones dysfunction

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ABSTRACT

Introduction and aim. Thyroid hormone abnormalities have been associated with oxidative changes in human beings. The aim of the study was to evaluate the oxidative stress marker and antioxidants status in individuals with thyroid hormone dysfunction in Ekiti State.

Material and methods. A total of eighty samples were recruited in this study comprising forty subjects with thyroid hormones dysfunction and forty apparently healthy controls. Malondialdehyde (MDA), reduced glutathione (GSH) and catalase were determined spectrophotometerically.

Results. MDA was non-significantly higher (p>0.05) in subjects (4.33±0.84 nmol/mL) compared with control (4.12±0.63 nmol/mL), catalase was non-significantly higher (p>0.05) in subjects (199.36±20.21 µm/mL) compared with control (181.55±16.61 µm/mL), while GSH was significantly lower (p<0.05) in subjects (79.31±10.12 µmol/mL) compared with control (127.21±7.29 µmol/mL).

Conclusion. It can be concluded that the increase in the reactive oxygen species accompanied with impairment of the antioxidant system occurs in patients with thyroid hormone dysfunction. Hypothyroidism and hyperthyroidism induces disequilibrium of the oxidative/anti-oxidative balance that can lead to subsequent development of inflammation and associated diseases.

Keywords. antioxidants, dysfunction, malondialdehyde, oxidative stress, thyroid hormone

Introduction

The thyroid gland produces thyroid hormones that are essential for the healthy development of body organs. The thyroid is a significant endocrine gland since it essentially controls how quickly metabolism occurs in the cells.[1] They are crucial for the mental and psychological growth of infants and young children. Thyroxine and L-triiodothyronine, which are referred to as T4 and T3 respectively, are two distinctive hormones secreted by the thyroid gland.[2] Hypothyroidism is referred to a deficiency in thyroid hormone secretion and action. Between 2% and 15% of the population suffers from this disorder, which can be minor or severe.[3] Hyperthyroidism arise from over secretion of thyroid hormone from the thyroid gland or extra thyroidal tissues which can be generally divided into primary and secondary variants.[4] The incidence of hyperthyroidism is about 3 per thousand and women are 8 times more likely than males to have it. Despite the availability of free T4 and free T3, hyperthyroidism is characterized by a reduction in blood thyrotropin levels, which leads to metabolic formation and an acceleration of free radical production, changing the activity of antioxidant enzymes.[5] The main components of oxidative metabolism are thyroid hormones.[6]

Oxidative stress, which is defined as a free radical/antioxidant imbalance favouring radicals, plays a role

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in the pathophysiology of numerous diseases and their consequences.[7] Reactive oxygen species (ROS) comprising of superoxide, hydrogen peroxide and hydroxyl radicals, have traditionally been thought to have the ability to cause cancer and enhance invasiveness. Under physiological conditions, production of ROS is controlled by a large quantity of antioxidant systems which proceed as protective mechanisms. These systems comprise of antioxidant enzymes including superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase.[8]

Malondialdehyde (MDA)is one of by-products of lipid peroxidation and the most extensively researched marker of oxidative stress having a three-carbon molecular weight aldehyde.[9] Monitoring MDA levels in many biological systems can serve as a crucial marker of lipid peroxidation both in-vitro and in vivo for a variety of medical conditions.[10] Catalase is a typical enzyme present in all most all living things that are exposed to oxygen. Catalase is an essential antioxidant enzyme in charge of degradation of the reactive oxygen species and hydrogen peroxide to water and oxygen.[11] Glutathione (GSH) is a unique molecule that takes part in a wide range of metabolic, transport and detoxifying functions.[12] In addition to being a significant antioxidant, the cysteine residue of glutathione makes it the most prevalent low-molecular-weight thiol-containing peptide in most live cells. Reduced GSH and oxidized glutathione (GSSG) are the two distinct forms of intracellular glutathione.[13]

Fundamentally, oxidative stress is defined as an imbalance between the generation of oxidants and the protective actions of antioxidants, which may be brought on by normal metabolic processes or pathological situations.[14] ROS are produced as a byproduct during the synthesis of thyroid hormones. However, the body's antioxidant systems eliminate the ROS when the redox balance is normal, reducing oxidative damage.[15] On the other hand, some situations, such as thyroid gland inflammation and tumour cell growth, may change the equilibrium between ROS and antioxidant levels in favour of the former, which would then result in oxidative damage.[16] To stop or even manage a wide range of disease problems, appropriate antioxidant levels must be maintained. The various biochemical parameters associated with thyroid disease have been extensively studied, but little is known about the role of antioxidants and oxidative stress markers in thyroid disease. Furthermore, studies examining the state of antioxidants and markers of oxidative stress in individuals with thyroid hormone abnormalities are lacking in our study area.

Aim

This study was carried out to determine the oxidative stress marker and antioxidants status in individuals with thyroid hormone dysfunction in Ekiti State.

Material and methods

Study area

This study was carried out in Ikere. Ikere is the second most populous and principal city of Ekiti State, Nigeria. The area lies between latitudes 70 30' North of the equator and longitudes 50 14' East of the Greenwich meridian. The city has an area of 262 km^2 and population density of 778.3/km^2.

Study design

A cross sectional study design was employed in this study. Male and female individuals with thyroid hormone dysfunction between the ages of 15 and 45 years were recruited for this study.

Ethical approval for this study was obtained from the Ethics and Research Committee, Bamidele Olumilua University of Education, Science and Technology Ikere (BOUESTI), Ekiti State, Nigeria (BOUESTI/HREC/23/02/0112). Institutional permission/approval was also equally obtained. Informed consent was sought from each subject who participated in the study before the collection of sample.

Sample size

Sample size was determined using the formula:

$n = z^2pq / d^2$

Where; n – the desired sample size; z – is a constant given as 1.96; p – prevalence (2.6%); q – 1.0 – p; d – acceptable error (5%)

$n = (1.96^2 \times 0.026 \times (1 - 0.026)) / 0.05^2$

$n = 38.9 \approx 39$

Study population

The study population was individuals with thyroid hormone dysfunction visiting University Health Center, BOUESTI, Ekiti State. A total of eighty (80) individuals comprising of forty (40)subjects (individuals with thyroid hormone dysfunction) and forty (40) apparently healthy individuals (controls) were recruited for this study.

Inclusion criteria

Individuals with thyroid hormones dysfunction (hyperthyroidism and hypothyroidism) in the study area who gave their consent were included in this study.

Exclusion criteria

Individuals currently undergoing medications, tobacco smokers, alcohol drinkers, pregnant and lactating women, those using imunosuppressive drugs, those with underlying health conditions such as diabetics, HIV/AIDs and cardiovascular diseases etc. and those who did not give their consent were excluded from the study.

Sample collection

For each participant, about five millimeters (5 mL) of blood was collected via vein puncture and dispensed into plain bottle and allowed to clot. The serum was separated by centrifugation and carefully withdrawn into a pre-labeled tube for the determination of reduced glutathione, malondialdehyde and catalase activity. Specimens not tested immediately were stored at -20^{0}C.

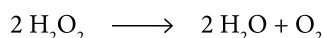
Analytical methods

Malondialdehyde, glutathione and catalase activities were determined spectrophotometrically using UV Visible spectrophotometer (PXUV-2601 model) manufactured by Panomex Inc., New Delhi, India.[11-13]

MDA is a product of lipid peroxidation. When heated with 2-thiobarbituric acid (TBA) under alkaline condition, it forms a pink coloured product, which has absorption maximum at 532 nm. The intensity of colour generated is directly proportional to the concentration of MDA in the sample.[11]

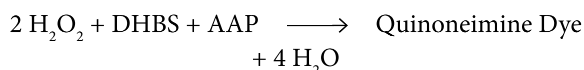
GSSG in the samples treated with trichloroacetic acid (TCA) solution was reduced with reagents including Sodium borohydride ($NaBH_4$)and sodium hydroxide (NaOH) to form GSH. NaOH was used to increase the pH, which was low due to the utilization of TCA solution, to enable the reduction of the GSSG molecules. $NaBH_4$ was used as a reductant. After the reduction was completed, hydrochloric acid (HCl) solution was added to remove the remnant $NaBH_4$ in order to prevent extra-reduction of Ellman's reagent (5,5'-dithiobis-(2-nitrobenzoic acid) (DTNB) molecules and re-oxidation of GSH molecules. GSH levels were measured using 500 mM Tris solution (pH=8.2). The thiol residues of GSH reduced the DTNB molecules to 2-nitro-5-benzoic acid which has an absorbance at 412nm spectrophotometrically. GSH was measured before and after the reduction process.[13]

The catalase activity in a sample is determined by measuring the decrease in hydrogen peroxide (H_2O_2) concentration observed following an incubation of the analyte sample with an H_2O_2 standard solution. Catalase reacts with a known quantity of H_2O_2. The reaction is stopped after exactly one minute with catalase inhibitor.



$$2\,H_2O_2 \xrightarrow{\text{Catalase}} 2\,H_2O + O_2$$

In the presence of peroxidase (HRP), the remaining H_2O_2 reacts with 3,5-Dichloro -2-hydroxybenzene sulfonic acid (DHBS) and 4-aminophenazone (AAP) to form a chromophore with a color intensity inversely proportional to the amount of catalase in the original sample.[12]



$$2\,H_2O_2 + \text{DHBS} + \text{AAP} \xrightarrow{\text{HRP}} \text{Quinoneimine Dye} + 4\,H_2O$$

Statistical analysis

All results were presented in tables and chat as mean ± standard deviation. Statistical analysis was done using one way analysis of variance (ANOVA) and Student's t-test using Statistical Package for Social Sciences (SPSS) version 25 (IBM, Armonk, NY, USA). Additionally, nonparametric Kruskal-Wallis test was used to verify the ANOVA-test results. A p-values <0.05 was considered significant.

Results

Table 1 showed the socio-demographic variable of the subjects and control group. The age (years) in mean ± SD of the subjects and control group was 35.36±5.61 and 36.10±4.64, while the body mass index (BMI) (kg/m^2) was 25.22±2.32 and 22.14±1.12 respectively. BMI was significantly higher (p<0.05) in subjects compared with control, but BMI did not show any significant difference (p>0.05). With respect to classification of thyroid dysfunction, 25 (62.5%) had hyperthyroidism, while 15 (37.5%) had hypothyroidism.

Figure 1 shows the mean values of thyroid stimulating hormone (TSH)andT3 in hypothyroidism, hyperthyroidism and control subjects. TSH was significantly higher (p<0.05) in hypothyroidism (10.86±1.59 mU/L) compared with control group (3.36±0.55 mU/L) and hyperthyroidism (1.12±0.15 mU/L), and in control group compared with hyperthyroid group. T3 was significantly higher (p<0.05) in hyperthyroid subjects (2.91±0.34 nmol/L) compared with hypothyroid subjects (1.46±0.22 nmol/L) and control subjects (1.51±0.26 nmol/L) respectively.

Figure 2 shows the mean values of thyroxine (T4) in hypothyroidism, hyperthyroidism and control subjects. T4 was significantly higher (p<0.05) in hyperthyroidism (155.12±22.31 nmol/L) compared with hypothyroidism (89.33±12.21 nmol/L) and control subjects (96.58±10.34 nmol/L) respectively.

Table 2 presents the antioxidants and oxidative stress parameter of subjects and control. The mean value of MDA (nmol/mL) in subjects and control was 4.33±0.84 and 4.12±0.63, Catalase (μm/mL) was 199.36±20.21 and 181.55±16.61, while reduced glutathione (μmol/mL) was 79.31±10.12 and 127.21±7.29 respectively. MDA and catalase were non-significantly higher (p>0.05) in subjects compared with control, while reduced glutathione was significantly lower (p<0.05) in subjects compared with control.

Table 3 shows the antioxidants and oxidant stress parameters of male and female subjects. The mean MDA (nmol/mL) levels of male (4.76±0.86) was non-significantly higher (p>0.05) compared with female subjects (4.13±0.79). Catalase (μm/mL) activity was non-significantly higher in male subjects (221.41±31.56) in comparison with female subjects (186.17±28.50). On the other

hand, reduced glutathione (µmol/mL) level was non-significantly higher in female subjects (80.21±10.61) compared with male subjects (73.44±15.24).

Table 4 presents the antioxidants and oxidative stress parameter of subjects with hyperthyroidism and hypothyroidism. The mean values of MDA (nmol/mL) was significantly higher ($p<0.05$) in subjects with hypothyroidism (6.34±1.39) compared with subjects with hyperthyroidism (4.89±1.12). Catalase (µm/mL) was significantly higher ($p<0.05$) in subjects with hyperthyroidism (248.33±26.48) compared with hypothyroidism (126.24±11.72). GSH (µmol/mL) was significantly higher ($p<0.05$) in subjects with hyperthyroidism (93.26±9.69) in comparison with hypothyroidism (56.77±8.36).

Table 5 shows the correlation between T3, T4 and TSH hormone levels and oxidative stress parameters in subjects. The results obtained showed that there was a significant positive correlation between T3 and MDA (r=0.802, p=0.000), T3 and catalase (r=0.760, p=0.001), T3 and reduced glutathione (r=0.786, p=0.001), and T4 and catalase (r=0.727, p=0.026) respectively.

Table 1. Socio-demographic variable of the subjects and control group*

Variable	Subjects (%) (n=40)	Control (%) (n=40)	p
Male	15 (37.5%)	14 (35%)	
Female	25 (62.5%)	26 (65%)	
Age (Mean ± SD) (years)	35.36±5.61	36.10±4.64	0.612
BMI (Mean ± SD) (kg/m²)	25.22±2.32	22.14±1.12	0.001*
Marital status			
Single	12 (30%)	25 (62.5%)	
Married	28 (60%)	15 (37.5%)	
Educational status			
Primary	2 (5%)	1 (2.5%)	
Secondary	18 (45%)	22 (55%)	
Tertiary	20 (50%)	19 (47.5%)	
Occupation			
Students	8 (20%)	15 (37.5%)	
Self-employed	18 (45%)	12 (30%)	
Civil servants	9 (22.5%)	10 (25%)	
Unemployed	5 (12.5%)	3 (7.5%)	
Classification of thyroid dysfunction			
Hyperthyroidism	25 (62.5%)	–	
Hypothyroidism	15 (37.5%)	–	

*BMI – body mass index, % – percentage, SD – standard deviation

Table 2. Antioxidant and oxidative stress parameter of subjects and control

Parameters	Subjects Mean±SD	Control Mean±SD	t	p
MDA (nmol/mL)	4.33± 0.84	4.12 ± 0.63	0.675	0.369
Catalase (µm/mL)	199.36 ± 20.21	181.55 ± 16.61	1.019	0.115
GSH (µmol/mL)	79.31± 10.12	127.21 ± 7.29	4.133	<0.0001

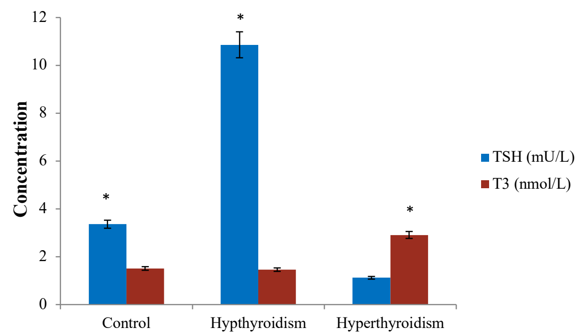


Fig 1. TSH and T3 in hypothyroidism, hyperthyroidism and control subjects (values with * significantly differ from other groups at $p<0.05$)

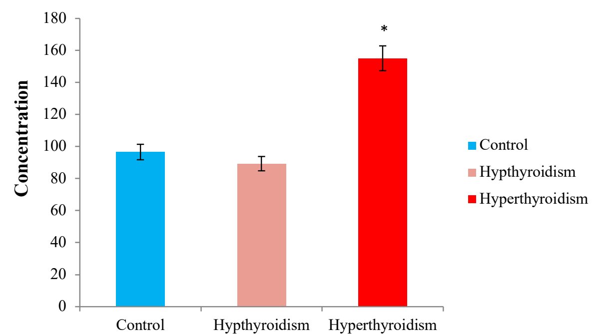


Fig 2. T4 in hypothyroidism, hyperthyroidism and control subjects (values with * significantly differ from other groups at $p<0.05$)

Table 3. Antioxidants and oxidative stress parameter of male and female subjects

Parameters	Male Mean±SD	Female Mean±SD	p
MDA (nmol/mL)	4.76±0.86	4.13±0.79	0.512
Catalase (µm/mL)	221.41±31.56	186.17±28.50	0.072
GSH (µmol/mL)	73.44±15.24	80.21±10.61	0.068

Table 4. Antioxidant parameters and oxidative stress parameter of Subjects with hyperthyroidism and hypothyroidism*

Parameters	Control Mean±SD	Hyperthyroidism Mean±SD	Hypothyroidism Mean±SD	p
MDA (nmol/mL)	$4.12±0.63^{a}$	$4.89±1.12^{b}$	$6.34±1.39^{c}$	0.412^{a+b} 0.003^{a+c} 0.002^{b+c}
Catalase (µm/mL)	$181.55±16.61^{a}$	$248.33±26.48^{b}$	$126.24±11.72^{c}$	0.002^{a+b} 0.001^{a+c} $<0.000^{b+c}$
GSH (µmol/mL)	$127.21±7.29^{a}$	$93.26±9.69^{b}$	$56.77±8.36^{c}$	$<0.000^{a+b}$ $<0.000^{a+c}$ 0.001^{b+c}

* values are statistically significant at $p<0.05$; $^{a+b}$ – represent control group vs hyperthyroid group, $^{a+c}$ – represent control vs hypothyroid group; $^{b+c}$ – represents hyperthyroid vs hypothyroid group

Table 5. Correlation between T3, T4 and TSH hormone levels and oxidative stress parameters in subject[a]

Variables	T3 r (p)	T4 r (p)	TSH r (p)
MDA	0.802 (<0.001)**	0.005 (0.990)	0.062 (0.874)
Catalase	0.760 (0.001)**	0.727 (0.026)*	-0.176 (0.652)
GSH	0.786 (0.001)**	0.177 (0.649)	-0.099 (0.799)

[a]** – correlation is significant at the level 0.01 level (2-tailed); * – correlation is significant at the level 0.05 level (2-tailed), r – Pearson's correlation

Discussion

This study was carried out to assess the oxidative stress marker and antioxidants status of individuals with thyroid hormone dysfunction in Ekiti State. In this study, MDA was non-significantly higher ($p>0.05$) in subjects compared with control. This increase could be the result of altered metabolic rates that produce too much H_2O_2 and nitric oxide.[17] Additionally, increased lipid peroxidation and the depletion of the body's antioxidant defense system may contribute to the rise in free radicals seen in thyroid dysfunction.[18] Elevated levels are observed in ROS-damaged tissues, as the final product of peroxidation, making them markers of oxidative stress in the body.[19] The increase in MDA found in this study is a sign of oxidative stress and lipid peroxidation. It's possible that the test subjects' oxidative stress was reduced by the action of catalase which was slightly elevated. This finding is agreement with previous research.[6,20-21] According to Basant et al., serum enzyme activities of MDA levels are good indicators for the systemic oxidant/antioxidant status, but they do not always correspond to changes that really occur in the thyroid directly.[6] This is because many different factors might affect the serum result.[6] In comparison to samples from normal thyroid tissue, the specimens from papillary carcinoma had significantly greater lipid peroxide concentrations expressed as MDA concentration.[20] In their investigation, Terziogluet al. observed that MDA levels before thyroidectomy were higher in thyroid dysfunction patients than in controls of same age, indicating enhanced free radical generation.[21]

The result of this study showed that catalase activity was non-significantly higher ($p>0.05$) in subjects compared with control. This research suggests an imbalance between antioxidants and oxidants in relation to aberrant thyroid function. ROS are produced more frequently as a result of changes in thyroid secretions. In the thyroid gland, free radicals and ROS play a role in both normal and pathological processes. ROS or free radicals are used by the endocrine system in the production of hormones. Since thyroid cells release enzymes that catalyse ROS production, the body's defence mechanisms and non-enzymatic antioxidants play a crucial role in neutralising excess ROS that isn't needed to produce thyroid hormones thereby maintaining overall homeostasis.[19] The thyroid hormone can control levels of enzymatic antioxidants including *superoxide dismutase*, glutathione peroxidase, catalase, and glutathione reductase as well as nonenzymatic antioxidants like vitamin E and C, glutathione, and uric acid, which can also influence the oxidative metabolism.[22]This finding is in agreement with previous studies which reported an increase in catalase activity in patients with thyroid dysfunction.[19,22-23] However dissimilar findings, showing markedly increased catalase in patients with thyroid dysfunction has also been described in literature when compared to controls.[24] Variations in ethnicity and dietary or ecological differences may be responsible for the discrepancy in findings. Additionally, the variation in antioxidant activity is tissue-specific and the reactions of antioxidant enzymes are not always the same.[25]

In this study, reduced GSH level was significantly lower ($p<0.05$) in subjects compared with control. Antioxidants can combat free radicals and neutralize oxidants. The lower levels of reduced glutathione as seen in this study may be due to its involvement in neutralizing and counteracting the effect of free radicals and oxidative stress occasioned by thyroid hormone dysfunction in our subjects. Reduced glutathione, an essential intracellular antioxidant, works as both a co-factor for glutathione peroxidase and a direct active scavenger to eliminate reactive species like the hydroxyl radical, carbon-centered radicals, peroxynitrite and singlet oxygen .[18]The protection of erythrocytes from oxidative damage is another highly important function of reduced GSH. It is a crucial antioxidant enzyme needed to neutralize ROS in different cell compartments and to respond to demanding circumstances. This finding is in consonant with previous studies which reported significant lower GSH levels in patients with thyroid gland dysfunction compared with healthy control.[17,19,22,24]

With respect to gender, MDA and catalase was non-significantly higher in males compared with female subjects, while reduced GSH level was non-significantly higher in female subjects compared with male subjects. According to a study, young men exhibit higher levels of in vivo oxidative stress indicators than women of the same age.[26] The generation of ROS was also shown to be higher in male vascular cells than female vascular cells.[27] Furthermore, research from both clinical and experimental settings revealed that women have a higher antioxidant potential than men.[28] According to these studies, there is a possible link between oxidative stress and gender, with women appearing to be less vulnerable.[26] ROS generation and the antioxidant defense system must be out of balance for oxidative stress to occur. The expression and/or activity of antioxidant enzymes appear to differ between males and females.[29]

In this study, MDA and catalase was significantly higher ($p<0.05$) in subjects with hypothyroidism com-

pared with hyperthyroidism, while reduced GSH was significantly higher in subjects with hyperthyroidism when compared with hypothyroid subjects. Both hyperthyroidism and hypothyroidism have been demonstrated to be related to oxidative stress. However, these two clinical diseases have different ways of producing oxidative stress: In hyperthyroidism, ROS generation is elevated, and in hypothyroidism, antioxidant availability is reduced.[5] This finding is in tandem with previous studies.[30-33] GSH is responsible for preserving the redox balance of cells. Reducing ROS levels and combating oxidative stress are possible effects of raised GSH levels.[32] Long-term oxidative stress can be associated with cell damage because it exceeds the capacity of antioxidant synthesis by the target organs or extracellular.[33] Ramli et al. reported that the activity of antioxidant enzymes was lowered and the quantity of TBA-active lipid peroxidation products (MDA) was much higher in hyperthyroid tissue.[30] Joshi et al.also shown that patients with hypothyroidism had lower MDA levels than patients with hyperthyroidism.[31] They conclude that lipid peroxidation was higher patients with hyperthyroidism compared with hypothyroid patients.[31]

Increased T4 and T3 thyroid hormone concentrations in hyperthyroidism lead to a rise in baseline metabolic rate, increased oxygen consumption and the production of significant amounts of reactive oxygen species, which heighten oxidative stress.[34] The elevated plasma TSH content in hypothyroidism is what causes the rise in lipid peroxidation. H_2O_2 generation is enhanced by high plasma TSH concentrations. H_2O_2 is an essential component in the production of thyroid hormones. It serves as an acceptor of electrons produced during oxidative hormone production processes.[35] Nicotinamide adenine dinucleotide phosphate oxidase system located in the apical membrane of the thyroid cell is responsible for producing H_2O_2 in the thyroid gland. The free radicals that are present in hypothyroidism are enhanced by H_2O_2 levels. Increased levels of TSH, H_2O_2, free radicals, and antioxidants as well as excessive vascularization, free radicals, and antioxidant levels all play a role in the development of thyroid conditions, which can result in oxidative stress.[36]

In this study, there was a significant positive correlation between T3 and MDA (r=0.802, p=0.000), T3 and catalase (r=0.760, p=0.001), T3 and GSH (r=0.786, p=0.001), and T4 and catalase (r=0.727, p=0.026) respectively. Sultana et al. in their study reported that in patients with hyperthyroidism, oxidative stress markers and thyroid hormone levels significantly correlate, and these markers can be useful in the assessment of the disease's prognosis.[37] The thyroid glands inflammatory process produces an excessive amount of ROS and free radicals, which suppress the antioxidants and cause an imbalance of oxidants and antioxidants.[19] Enhancing antioxidant defences to restore the equilibrium through therapeutic interventions may be helpful in the management of patients with hyperthyroidism since the oxidant-antioxidant balance is crucial for the regular function of the thyroids.[19] In order to improve thyroid function and restore oxidant-antioxidant equilibrium in hyperthyroid individuals, antioxidant supplementation with antithyroid medications may be used.[37]

Conclusion

It can be concluded that the increase in the reactive oxygen species accompanied with impairment of the antioxidant system may occur in patients with thyroid hormone dysfunction. Our results suggest that thyroid hormones in excess may be accompanied by increase in oxidative stress and impairment of the antioxidant system especially in females. Further study with larger sample size is required. Hypothyroidism and hyperthyroidism induces disequilibrium of the oxidative/anti-oxidative balance that can lead to subsequent development of inflammation and many associated diseases. This can be prevented by the adequate management of the disease and supplementation with anti-oxidative dietetics. Thus, reduction of oxidative stress may be beneficial in patients with subclinical hypothyroidism.

Declarations

Funding

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Author contributions

Conceptualization, E.A.O.; Methodology, E.A.O. and O.D.A.; Validation, E.A.O. and O.D.A.; Formal Analysis, E.A.O. and O.D.A.; Resources, E.A.O. and O.D.A.; Writing – Original Draft Preparation, E.A.O.; Writing – Review & Editing, E.A.O. and O.D.A.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

Data available on request from the authors.

Ethics approval

Ethical approval for this study was obtained from the Ethics and Research Committee, Bamidele Olumilua University of Education, Science and Technology Ikere (BOUESTI), Ekiti State, Nigeria.

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