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Original Article

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Oxidative stress pattern of patients with abnormal thyroid function in Southern Nigeria

Festus Oloruntoba Okojie [1], Dic-Ijiewere Ebenezer Oseremen [1]*, Ailemen, Felix Eromosele [1], Imafidon Nathaniel Odiamehi [1,2], Ebo Joseph Osaro [2], Nwankwo Chikezie Chinedu [1,2], Iweka Friday Kenneth [1,2]

[1]*Department of Chemical Pathology, Ambrose Alli University, Ekpoma, Nigeria*

[2]*Department of Chemical Pathology, Irrua Specialist Teaching Hospital, Irrua, Nigeria*

***Corresponding author:** Dr. Dic-Ijiewere Ebenezer Oseremen, **Address:** Address: Department of Chemical Pathology, Ambrose Alli University, Ekpoma, Nigeria, **Email:** ebenexar@gmail.com, **Tel:** +2347030430785

Abstract

***Background & Aims*:** In humans, oxidative changes have been associated with abnormal thyroid hormone levels. The aim of the study was to evaluate antioxidants and oxidative stress parameters in subjects with abnormal thyroid hormones in Irrua, Edo State.

***Materials & Methods*:** Two hundred samples were used for this study including 120 test subjects visiting the clinic with abnormal thyroid-related complaints and 80 healthy control groups. The triiodothyronine (T_3), thyroxine (T_4), thyroid stimulating hormone (TSH), malondialdehyde (MDA), reduced glutathione (rGSH), and catalase levels were determined using standard laboratory procedures. The results were presented in tables and charts as mean ± standard deviation.

***Results*:** Analysis of oxidative stress markers revealed that MDA levels in test subjects (4.9 ± 0.6) were not significantly different from the control group (4.7 ± 0.5; $P = 0.77$). Similarly, catalase activity in test subjects (216.9 ± 25.8) showed no significant difference compared to controls (178.6 ± 19.4; $P = 0.29$). However, rGSH levels were significantly lower in test subjects (74.8 ± 9.7) compared to controls (134.6 ± 9.7; $p < 0.001$). When analyzing thyroid function parameters, females with normal thyroid function exhibited significantly higher serum catalase levels (283.1 ± 38.9) compared to those with subclinical hyperthyroidism (101.5 ± 8.4) or hyperthyroidism (131.9 ± 13.0; $P < 0.05$). Among male participants, those with hyperthyroidism showed significantly lower rGSH levels (77.3 ± 23.5) compared to both males with subclinical hypothyroidism (186.0 ± 00.0) and healthy male controls (136.8 ± 7.7; $P < 0.05$). A key finding from this study is that thyroid dysfunction may not cause oxidative stress through lipid peroxidation. However, by the suppression of rGSH, this can have severe implications on the overall antioxidant defense system of the body predisposing it to oxidative damage and diseases.

***Conclusion*:** The findings of this study show that hyperthyroidism induces oxidative stress regardless of gender, which could play a major role in disease formation and other associated abnormal conditions.

***Keywords*:** Catalase, Glutathione, Hormone, Malondialdehyde, Oxidative, Thyroid

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Introduction

A complex interplay occurs between the hormonal system, oxidative stress, and redox balance which affect various important biological processes and pathophysiological conditions (1). Comprehension of the interplay between hormones, oxidative stress, and

redox equilibrium in humans is not completely understood (2). The thyroid gland is a vital endocrine organ that secretes important hormones critical for cellular metabolism (3, 4). Individual growth of normal cells is greatly influenced by thyroid hormones. These hormones are vital for fetal and neonatal mental development (5). Two hormones are primarily secreted by the thyroid gland including triiodothyronine (T_3) and thyroxine (T_4) generated from the amino acid tyrosine (6). Reduced secretion of thyroid hormone results in the condition known as hypothyroidism a common non-severe or severe condition that affects ≤ 15% of a population (5). Increased secretion of thyroid hormone by the thyroid gland or other non-thyroid tissues, results in the condition known as hyperthyroidism that could primarily be a disorder originating from the thyroid gland or secondary hyperthyroidism originating from other non-thyroidal sources (4). These thyroid hormones constitute a significant oxidative influence (7, 8). Thyroid hormones constitute one of the major important oxidative metabolic factors (7, 9).

The thyroid exhibits its action on energy metabolism, consumption of oxygen, and some mitochondrial functions such as oxidative phosphorylation, and mitochondrial respiration which when increased leads to several changes in cellular activities of respiratory chain components of the mitochondrial. The thyroid hormone's activities cause an increase in superoxide and other free radicals generation in the transport system of the mitochondrial electron (10). The oxidative stress effect, which is characterized as an imbalance between free radicals and antioxidants in favor of radicals, participates in the pathogenesis of many diseases and their complications (11, 12). Reactive oxygen species (ROS) consisting mainly of superoxide, hydrogen peroxide (H_2O_2), and hydroxyl radical, have been conventionally considered to have carcinogenic potential and can promote invasiveness (12). The anti-oxidant enzymes which include catalase, glutathione peroxidase, superoxide dismutase, and glutathione reductase are very vital in the control and suppression of ROS formation in normal physiological conditions (12).

Glutathione is a special molecule that participates in a great variety of metabolic processes, transport, and detoxification (13). Other than being a valuable antioxidant, glutathione is the major low molecular weight thiol that contains peptide and cysteine residue that is in many living cells (14). The distinct forms of intracellular glutathione include oxidized glutathione (GSSG) and reduced glutathione (rGSH) (15). Its special characteristics facilitate its participation in many biological activities, among them, protection against free radicals damage, transferring amino acids into the cell, conjugation of toxic metabolites and compounds, cellular signaling, and regulation of proteins (14). It could be found as rGSH and GSSG, and the proportion between both species shows the capacity the cell has to cope with oxidative attacks (16). Their physiological functions are very varied: regulating protein synthesis, modifying enzymatic activity and protection against oxidative damage (17). The tri—carbon molecular weight aldehyde malondialdehyde (MDA) is a by-product of the peroxidation of lipids and the most studied and assessed index of oxidative stress (18). The monitoring of MDA levels in different biological systems can be used as an important indicator of lipid peroxidation both in-vitro and in vivo for various health disorders (19) During intracellular oxidative stress MDA generated in the cells reacts with DNA leading to MDA-DNA adducts formation, this confers its significance as a biomarker of cellular DNA damage (20). Determination of MDA in blood plasma or tissue homogenates is one of the useful methods to predict oxidative stress levels (21).

The common enzyme catalase is present in almost every living organism dwelling in an oxygenated environment. The enzyme catalase is a vital antioxidant which breakdown ROS and H_2O_2 to yield oxygen and water (22). This enzyme which is critical in reproductive reactions, is a four-polypeptide chain tetramer, with each longer than 500 amino acids. The 4 groups of porphyrin-heme are involved in the enzymatic reaction with H_2O_2 (23). Oxidative stress is basically characterized by a disruption in the balance between oxidant production and antioxidant protective responses

that may be induced during natural metabolic processes or pathologic conditions (24). Similarly, ROS are yielded in thyroid hormone production. However, under normal redox balance, the ROS are removed by antioxidant systems in the body, hence limiting oxidative damage. On the other hand, certain conditions such as inflammation of the thyroid gland as well as tumor cell proliferation could alter the balance between ROS and antioxidant levels in favor of the former, subsequently resulting in oxidative damage (25). Although biochemical indices in thyroidism have been studied, antioxidant and oxidative stress indices in thyroidism are not well documented (7). Furthermore, there are limited studies on the effect of abnormal thyroid hormone on oxidative stress markers (MDA, rGSH, and catalase) which necessitated this study. Hence, the objective of this study was to determine the pattern of oxidative stress induced by abnormal thyroid function by assessing the levels of anti-oxidative parameters such as rGSH and Catalase, as well as MDA an oxidative stress marker.

Materials & Methods

Study Area

This study was a hospital-based cross-sectional study, involving patients visiting Irrua Specialist Teaching Hospital, Irrua, in the southern part of Nigeria who consented to the study. This hospital serves as the training center for the medical school of Ambrose Alli University, Ekpoma, Nigeria.

Study Period

This study was undertaken between December 2023 and March 2024.

Study Subjects

There were 120 study subjects visiting the clinic with abnormal thyroid complaints between the ages of 15 and 65 years (60 males and 60 females). Eighty healthy individuals with normal thyroid function test values served as control subjects.

Inclusion Criteria

Study participants who willingly consented to their blood samples and biodata being collected were co-opted into this study.

Exclusion Criteria

Study participants on medications, regular alcohol consumers, tobacco users, lactating mothers and pregnant women, patients with HIV/AIDS, those with diabetes, and cardiovascular conditions, and those using immunosuppressive drugs, were all excluded from the study.

Ethical Permission and Informed Consent

Ethical permission was sought and obtained for this study from the Ambrose Alli University Ekpoma, Nigeria Health Ethics and Review Committee with the registration number, NHREC/12/06/2013/135/23. Informed consent was sought from each subject who participated in the study before the collection of blood samples.

For each participant, ten-milliliter blood samples were obtained from study participants through venipuncture and dispensed into the appropriate sample bottles and left to clot. The blood was separated by centrifuging the sample. Catalase, rGSH, and MDA were determined and when not tested immediately they were stored at 2-8C%.

Estimation of Test Parameters

Enzyme-linked immunosorbent assay technique using the Tecan infinite F50 ELISA microplate reader was utilized for the evaluation of thyroid stimulating hormone (TSH), T_3, and T_4 in the blood samples of test and control subjects. MDA was determined as a product of lipid peroxidation when heated with 2-thiobarbituric acid (TBA) under alkaline conditions, using the spectrophotometric method as originally described by Mihara & Uchiyama (26). The determination of rGSH in the samples was carried out using the spectrophotometric method that involves the reduction of 5, 5' –dithiobis (2-Ni-trobenzoic acid) (DTNB) to 2-nitro-5-benzoic by the thiol residues of rGSH as utilized by Weydert & Cullen (27). The activity of catalase was

determined in the sample by assessing the decrease in H_2O_2 levels following analytes incubation with an H_2O_2 standard solution as described by Weydert & Cullen (27).

Statistical Analysis

The results are shown in tables and chats as mean (± standard deviation) of control and test data. Laboratory data, with the aid of the Statistical Package for Social Sciences (SPSS) version 21.0 software, were used to carry out an analysis of variance and independent sample t-test. A *P-value* of ≤ 0.05 was considered significant.

Results

The results of the study are presented in figures and tables below. The results obtained showed that 6% of the study populations were females with subclinical hyperthyroidism, 27% were females with hyperthyroidism, 10% were females with subclinical hypothyroidism, 27% were ill females with normal thyroid function test (TFT), 10% were males with hyperthyroidism, 3% were males with subclinical hypothyroidism and 17% were ill males with normal TFT (Figure 1).

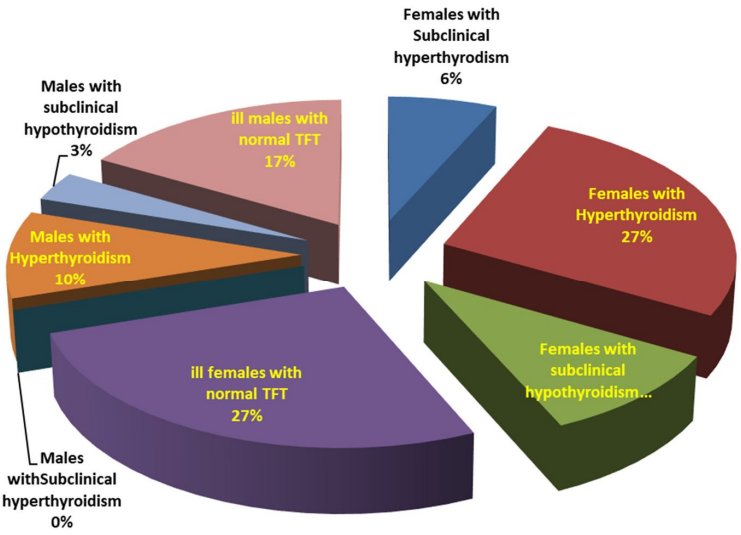

Fig. 1. Characteristics of the study population

- TFT: Thyroid function test
- Subclinical hyperthyroidism (TSH within 0.1-0.4 mIU/L and normal Total T3 and T4)
- Normal Thyroid function test (TFT): TSH of 0.4-4.0; Total T3 of 0.9 – 2.8 nmol/L; Total T4 of 57-149 nmol/L
- Subclinical hypothyroidism: TSH > 4.0 mIU/L with normal T3 and T4
- Hypothyroidism: TSH > 10 mIU/L with normal T3 and T4

Hyperthyroidism: TSH < 1.8 mIU/L with elevated T3 > 2.8 nmol/L and/or T4 > 150 nmol/L

Figure 2 shows the TSH and T_3 levels in male and female test subjects. The results obtained showed that the mean values of TSH in female and male subjects were 2.7 ± 1.0 and 1.7 ± 0.6, while T_3 (nm/L) was 1.6 ± 0.2 and 1.4 ± 0.2 respectively. There was no significant difference ($P > 0.05$) in the TSH and T_3 of male subjects compared with female subjects.

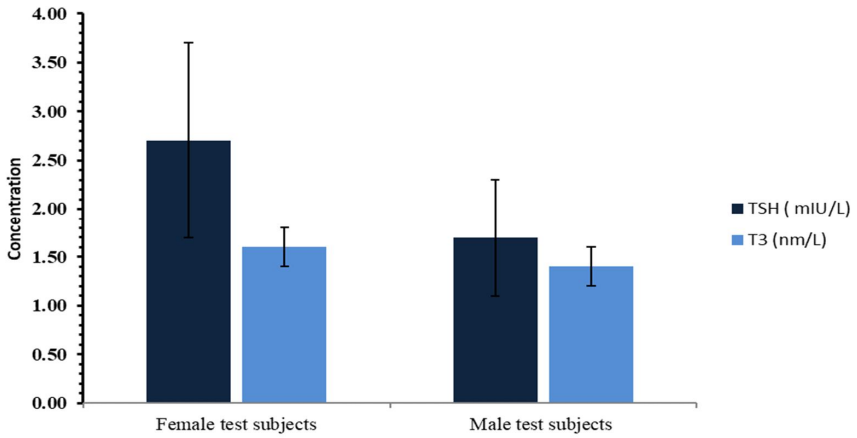

Fig. 2. TSH and T_3 levels in male and female test subjects

Figure 3 shows the T_4 levels in male and female test subjects above and below 45 years of age. From the results obtained, the TSH (nm/L) of female test subjects below 45 years (164.4 ± 15.6) in comparison with female test subjects above 45 years of age (117.2 ± 13.0) was significantly lower ($P = 0.036$). The TSH (nm/L) of male test subjects below 45 years (105.1 ± 12.7) in comparison with male test subjects above 45 years of age (155.1 ± 28.2) was non-significantly lower ($P>0.05$). * Mean value is significantly lower than female test subjects < 45 years of age ($p = 0.036$).

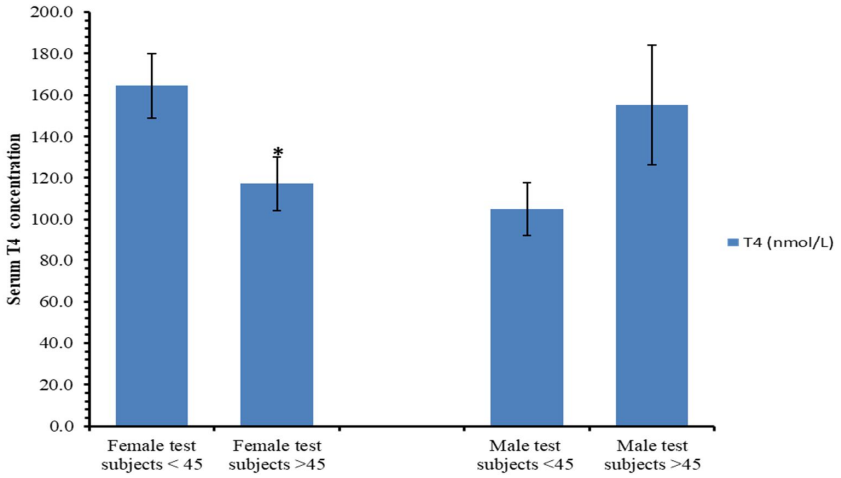

Fig. 3. T_4 levels in male and female test subjects above and below 45 years of age

Table 1 shows the antioxidant and oxidative stress parameters of test subjects in comparison with the control group. The results obtained showed that in test subjects and control group, MDA levels were 4.9 ± 0.6 and 4.7 ± 0.5, catalase levels (µm/mg protein) were 216.9 ± 25.8 and 178.6 ± 19.4, while rGSH levels (µmol/ml) were 74.8 ± 9.7 and 134.6 ± 9.7, respectively.

Table 1. Oxidative stress and antioxidant indices of study participants with abnormal thyroid function parameters (Test) in comparison with the control group

Parameters	Test (n = 120)	Control (n = 80)	*P-value*	Significance	Parameters
MDA (µm/mg protein)	4.9 ± 0.6	4.7 ± 0.5	0.77	NS	MDA (µm/mg protein)
Catalase (µ/mg protein)	216.9 ± 25.8	178.6 ± 19.4	0.29	NS	Catalase (µ/mg protein)
rGSH (µmol/ml)	74.8 ± 9.7	134.6 ± 9.7	0.00*	S	rGSH (µmol/ml)

*Significant at $p \leq 0.05$

NS: Not significant; S: Significant

Table 2 shows the antioxidant and oxidative stress parameters of male and female test subjects in comparison with the male and female control groups. The results obtained showed that the mean MDA levels of male control subjects (4.1 ± 1.1) and female control subjects (4.9 ± 0.6) were not statistically significant in comparison with female test participants (4.7 ± 0.7) and male test participants (5.5 ± 1.1) (P = 0.82). Also, the rGSH levels of female control (133.5 ± 13.9) and male control subjects (136.8±11.4) were significantly higher than female test subjects (77.9 ± 11.3) (P = 0.00; P = 0.00) and male test subjects (67.5 ± 19.7) (P = 0.00; P = 0.00). Catalase levels of male control subjects (147.0 ± 34.1) and female control subjects (195.6 ± 23.2) were not statistically significant in comparison with female test participants (199.7 ± 31.8) and male test participants (256.9 ± 43.4) (P = 0.37).

Table 2. Some oxidative stress and antioxidant indices of males and females with abnormal thyroid function parameters (Test) in comparison with the male and female control groups

Parameters	Female control subjects (n = 40)	Male control subjects (n = 40)	Female test subjects (n = 60)	Male test subjects (n = 60)	*P-value*
MDA (µm/mg) protein	4.9 ± 0.6[a]	4.1 ± 1.1[a]	4.7 ± 0.7[a]	5.5 ± 1.1[a]	0.82
Catalase (µ/mg) protein	195.6 ± 23.2[a]	147.0 ± 34.1[a]	199.7 ± 31.8[a]	256.9 ± 43.4[a]	0.37
rGSH (µmol/ml)	133.5 ± 13.9[a]	136.8 ± 11.4[a]	77.9 ± 11.3[b]	67.5 ± 19.7[b]	0.00*

*Significant at $p \leq 0.05$.

Table 3 shows the oxidative stress and antioxidant indices of female study participants with normal and abnormal Thyroid function. The increase in activity of catalase was statistically significant in unhealthy females that had normal TFT, followed by females with subclinical hypothyroidism when compared with other groups. On the other hand, rGSH was significantly higher ($P < 0.05$) in healthy female control subjects and females with subclinical hypothyroidism compared with other groups. There was no significant difference in MDA in all the groups studied when compared with healthy female control subjects.

Table 3. Some oxidative stress and antioxidant indices of Female study participants with normal and abnormal Thyroid function

Indices	Healthy female control subjects	Unhealthy females with normal TFT	Females with subclinical hyperthyroidism	Females with hyperthyroidism	Females with subclinical hypothyroidism	*P-value*
MDA (µm/mg protein)	5.0 ± 0.4	4.2 ± 0.7	7.3 ± 0.8	5.0 ± 0.9	3.5 ± 1.5	0.256
Catalase (µ/mg protein)	195.6 ± 16.1[a]	283.1 ± 38.9[b]	101.5 ± 8.4[a]	131.9 ± 13.0[a]	223.6 ± 85.2[ab]	0.003*
rGSH (µmol /ml)	133.5 ± 9.7[a]	80.0 ± 11.4[b]	47.3 ± 4.2[b]	74.8 ± 14.4[b]	101.2 ± 25.3[ab]	0.001*

*Statistically Significant at $p \leq 0.05$. Values are Mean ± Standard deviation.

- Values with one different superscript are statistically significant at $P \leq 0.05$.
- Subclinical hyperthyroidism (TSH within 0.1-0.4 mIU/L and normal Total T3 and T4).
- Normal Thyroid function test (TFT): TSH of 0.4-4.0; Total T3 of 0.9–2.8 nmol/L; Total T4 of 57-149 nmol/L.
- Subclinical hypothyroidism: TSH > 4.0 mIU/L with normal T_3 and T_4
- Hypothyroidism: TSH > 10 mIU/L with normal T3 and T4.

Hyperthyroidism: TSH < 1.8 mIU/L with elevated T3 > 2.8nmol/L and/or T4 > 150 nmol/L.

Table 4 shows the oxidative stress and antioxidant indices of male study participants who had normal and abnormal thyroid function. The mean MDA level was significantly increased in unhealthy males that had normal TFT, followed by males with hyperthyroidism when compared with healthy male control subjects and males with subclinical hypothyroidism. The activity of catalase was significantly increased in male study participants with subclinical hypothyroidism and followed by males with hyperthyroidism when compared to healthy male control and unhealthy males with normal TFT. Also, rGSH was significantly higher ($P < 0.05$) in males with subclinical hypothyroidism followed by male control when compared with unhealthy males with normal TFT and males with hyperthyroidism respectively.

Table 4. Some oxidative stress and antioxidant indices of male study participants having normal and abnormal thyroid function

Parameters	Healthy male control subjects	Unhealthy males with normal TFT	Males with hyperthyroidism	Males with subclinical hypothyroidism	*P-value*
MDA (µm/mg protein)	4.1 ± 0.7[ab]	6.3 ± 0.7[a]	5.8 ± 1.6[a]	1.0 ± 0.1[b]	0.048*
Catalase (µ/mg protein)	147.0 ± 43.2[a]	208.9 ± 40.1[ab]	314.0 ± 50.0[b]	326.0 ± 00.0[b]	0.012*
rGSH (µmole /ml)	136.8 ± 7.7[a]	37.9 ± 4.7[b]	77.3 ± 23.5[c]	186.0 ± 00.0[a]	0.000*
rGSH (µmole /ml)	136.8 ± 7.7[a]	37.9 ± 4.7[b]	77.3 ± 23.5[c]	186.0 ± 00.0[a]	0.000*

*Statistically significant

- Values are Mean ± Standard deviation. Values with varying superscript are statistically significant at $P \leq 0.05$.
- Subclinical hyperthyroidism (TSH within 0.1-0.4 mIU/L and normal Total T3 and T4).
- Normal Thyroid function test (TFT): TSH of 0.4-4.0; Total T3 of 0.9 – 2.8 nmol/L; Total T4 of 57-149 nmol/L.
- Subclinical hypothyroidism**:** TSH > 4.0 mIU/L with normal T_3 and T_4
- Hypothyroidism: TSH > 10 mIU/L with normal T3 and T4.

Hyperthyroidism: TSH < 1.8 mIU/L with elevated T3 > 2.8 nmol/L and/or T4 > 150 nmol/L.

Discussion

The occurrence of oxidative stress characterizes many biological and pathological processes (12). This study showed a non-significant increase in MDA and Catalase in test subjects compared with the control group. From a previous study, it has been observed that the activity of MDA is a good indication of oxidative activities in the thyroid but not the actual changes taking in the thyroid directly, because numerous factors are involved and can modify the serum outcome (7). Sadani and Nadkarni (28) showed that lipid peroxide concentration, expressed as MDA concentration, was significantly higher in the specimens from papillary carcinoma than those in the normal thyroid tissue. The increase of free radicals in thyroid cancer conditions is suggested to be due to the increased lipid peroxidation and the damage of the antioxidant defense system (29). In a study, Akinci et al. (30) reported that in thyroid cancer patients MDA levels before thyroidectomy were found to be higher than those in age-matched control subjects indicating increased free radical generation. The increased MDA in test subjects with abnormal thyroid hormones than healthy control subjects in this study which is indicative of lipid peroxidation and oxidative stress. This finding of increased MDA in thyroid disorder agrees with the study of Sultana et al. (31) and Varghese et al. (32), which also reported decreased total antioxidant capacity (TAC) in the abnormal thyroid subjects. When antioxidants such as TAC, catalase, and rGSH are reduced, it is also indicative of oxidative stress. From Table 1, there is slight oxidative stress characterized by increased MDA and decreased rGSH. This oxidative stress in test subjects in this study may have been ameliorated by the effect of catalase which was slightly increased.

In this study, there was no significant difference (P<0.05) in the MDA of males compared with females in both test and control subjects. Furthermore, although there was no significant difference (P < 0.05) in the MDA of healthy female control subjects compared with unhealthy females with normal TFT, females with subclinical hyperthyroidism, females with hyperthyroidism, and females with subclinical hypothyroidism, MDA level was markedly higher in females with subclinical hyperthyroidism, and this could be due to the corresponding lowest antioxidant status of these study participants. However, increased MDA levels were recorded in unhealthy males that had normal TFT, followed by males with hyperthyroidism when compared with healthy male control subjects and males with subclinical hypothyroidism. In the current study, there was a significant increase in MDA levels in all groups of patients with thyroid disorders compared to the level of the control group. This aligns with the report of Kochman et al. (33) which reported oxidation of lipids in the human thyroid gland and increased product of active TBA lipid peroxidation (MDA) in hyperthyroid tissue and the action of antioxidant enzymes (catalase, GSHPx) was decreased. Marcocci et al. (34) have also reported increased oxidative stress hyperthyroidism from Grave's disease. Similar studies by Joshi et al. (35) also showed that MDA increased in the hyperthyroid patients, as compared to the hypothyroid, euthyroid patients and control subjects, which could be indicative of a high rate of lipid peroxidation during hyperthyroidism, which aligns with our study which was able to further establish the particular hyperthyroid condition involved and gender influence, as there was marked increase in MDA in female subjects with subclinical hyperthyroidism. This oxidative stress in females with subclinical

hyperthyroidism could be attributable to an increased oxygen consumption, and increased lipid peroxidation from high intracellular ATP consumption. Previous studies have shown that free radical production and lipid peroxidation were related to hypermetabolic state in hyperthyroid females (36, 37). There has been no particular pattern from previous reports on hyperthyroidism-induced oxidative stress. It was recorded in related research that lipid peroxidation product (MDA) was reduced (38, 39). In contradiction, the studies of Omon et al. (36) and Kumari et al. (40) reported increased levels of lipid peroxidation in female patients. In a related study also, decreased levels of MDA in hyperthyroid female subjects were found by Iangalenko et al. (41).

Malondialdehyde was increased significantly ($P < 0.05$) in unhealthy males that had normal TFT, followed by males with hyperthyroidism when compared with healthy male control subjects and males with subclinical hypothyroidism. This could be an indication of oxidative stress occasioned by non-thyroidal causes in these males with normal thyroid function, and this may also play a significant role in creating a disease state. In previous studies, different interpretations were given. It was demonstrated that thyroxin decreased the concentration of the products of lipid peroxidation in animal experiments (35, 36). Kumari et al. (40) recorded increased plasma MDA concentration in individuals having hyperthyroidism in variance with their control. Costantini et al. (42) demonstrated that hyperthyroidism can stimulate lipid peroxidation. Iangolenko et al. (41) observed an increase in MDA levels in hyperthyroidism. Adali et al. (43) found that lipid peroxidation was increased in hyperthyroid individuals.

High levels of ROS which induces oxidative stress is observed in hyperthyroidism as elevated levels of thyroid hormones T_3 and T_4 lead to increased oxygen consumption and high metabolic rate (44). Elevated levels of thyroid stimulating hormone in plasma can result in higher levels of lipid peroxidation in hypothyroid patients. H_2O_2 levels are increased with increased serum thyroid stimulating hormone concentration. In thyroid hormone production, H_2O_2 is a critical factor, due to its capacity to accept electrons produced during hormone synthesis-induced oxidative reactions (44).

The findings of increased catalase in this study indicate a bit of oxidant/antioxidant imbalance associated with abnormal thyroid function. This finding is in agreement with a previous study by Seyed-Mostafa et al. (45) who reported an increase in the activities of catalase in thyroid dysfunction patients. Enzymatic antioxidants such as MDA, Catalase, and superoxide dismutase are valuable indicators of systemic oxidative activities, although a lesser indicator of prevailing changes in the thyroid as a result of several factors that can alter serum levels. The thyroid hormone regulates oxidative metabolism by influencing the levels of antioxidants such as catalase, superoxide dismutase, and rGSH, antioxidants like vitamin C, E, and uric acid that are non-enzymes (45).

Furthermore, catalase was increased significantly ($P< 0.05$) in unhealthy females having normal TFT, followed by females with subclinical hypothyroidism when compared with other groups. Catalase was increased significantly ($P < 0.05$) in males having subclinical hypothyroidism followed by males with hyperthyroidism when compared to healthy male control subjects and unhealthy males with normal TFT. Hyperthyroidism seems to confer more oxidative stress than hypothyroidism in females. This outcome aligns with previous findings (46). In agreement with our findings, Olio et al. (47) showed that some antioxidants were decreased and malondialdehyde was decreased in subjects with hyperthyroidism. This affirms the hypothesis that hyperthyroidism plays an intricate role in oxidative stress formation. Free radicals have been seen to play a vital role in the initiation process of many neoplastic transformations both in vitro and in vivo as well as the formation of specific oncogenes (45). Findings from this study showed a significant decrease in glutathione levels of ill subjects (test subjects) than in the healthy control subjects. The decline in rGSH has been reported also in similar studies on thyroid gland dysfunction (45, 46, 48). Glutathione (reduced form) is

very important in the protection of red blood cells against oxidative destruction (49).

Furthermore, rGSH was significantly higher in males with subclinical hypothyroidism followed by male control subjects when compared with unhealthy males with normal TFT and males with hyperthyroidism respectively. On the other hand, rGSH was significantly higher ($P < 0.05$) in healthy female control subjects and females with subclinical hypothyroidism compared with other groups. This aligns with the findings of Senat et al. (50). There was no significant difference in the TSH and T_3 levels of male subjects compared with female subjects. However, TSH was significantly lower ($P < 0.05$) in female test subjects less than 45 years of age ($P = 0.036$) compared to female subjects above 45 years. Hyperthyroidism and hypothyroidism observed in the study could induce changes in antioxidant defense mechanisms leading to tissue damage and imbalance in thyroid hormones.

Conclusion

In conclusion, it can be seen that hyperthyroidism and hypothyroidism are characterized by alterations in the antioxidant system which is predicated on the observed increased reactive oxygen species. The significant alterations in anti-oxidative and oxidative stress indices in hyperthyroidism could lead to the production of ROS which could cause oxidative damage to heart muscles and other cellular structures of the body and play a major role in disease formation and other associated abnormal conditions. A key finding from the result of this study is that thyroid dysfunction does not lead to oxidative stress through lipid peroxidation as recorded from the non-significant difference in MDA of test and subjects, but by the suppression of antioxidant defense systems such as rGSH. Increased oxidative stress and decreased antioxidant capacity may be associated with worsening thyroid function in hyperthyroid patients, especially females. Antioxidant supplementation in hyperthyroid females could exert some beneficial effects and cause a decline in ROS.

Acknowledgments

None declared.

Ethical statement

Ethical approval for the study was obtained from the Ethics and Review Committee of Ambrose Alli University, Ekpoma, Nigeria with the registration number, NHREC/12/06/2013/135/23.

Data availability

None declared.

Conflict of interest

There is no conflict of interest among the authors.

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Author contributions

None declared.

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