

**A CASE CONTROL STUDY OF OXIDATIVE STRESS IN TYPE 2 DIABETES  
MELLITUS PATIENTS WITH HYPERTENSION ATTENDING JOS UNIVERSITY  
TEACHING HOSPITAL (JUTH), NIGERIA**

**Abstract**

Diabetes is a serious, long-term condition with a major impact on the lives and wellbeing of individuals, families, and societies worldwide. Also, oxidative stress is associated with the pathogenesis of diabetes mellitus and many other diseases, in this study a random selection was done for 54 subject's male and female, having two groups, control and test group. The aim of this study was to investigate the status of oxidative stress and antioxidant enzymes related parameters in type 2 diabetes mellitus patients (T2DM) with hypertension attending Endocrinology unit at Jos University Teaching Hospital (JUTH). A total of 27 patients who had been diagnosed with type 2 diabetes (T2DM) with hypertension and 27 healthy individuals who volunteer and were recruited into the study). The parameters use for the evaluation of the oxidant was Malondialdehyde (MDA) which is a marker for lipid peroxidation, Glycated hemoglobin (HbA1c) and Lipid profile. Antioxidant enzymes parameters which included superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) were also examined. HbA1c level was statistically significantly higher in diabetic patients as compared to those of healthy participants. Demographic study which included lifestyle and Clinical assessment was also carried out. Higher levels of MDA activity was observed in the diabetic group compared to those of the healthy participants having a  $P = 0.001$ . There was also an increased activity in SOD, CAT and GSH in the diabetic group as compared to the control group with  $P = 0.001$ . Among those who exercised both in the diabetic and the non- diabetic group there was a significant difference statistically ( $P$  value of 0.001) in lipid profile compared to those that did not exercise and same was applicable to those who were diabetic and had a session with the registered dietician and those that did not. In the Lipid profile assessment, it was noteworthy that the diabetics that exercised regularly and had a session with a dietician or Endocrinologist had significantly higher HDL compared to those that did not. Changes in many of the measured risk factors that occurred in test group compared with control group may provide an explanation of how type 2 diabetes mellitus progresses with free racial oxidative stress biomarkers and future complications can be minimize.

**1.0: Introduction**

Free radicals are highly reactive chemical entities that exist for a short period of time [1] and contain one or more unpaired electrons [2]. While they can be seen as necessary for signaling in

normal processes like cell differentiation and migration [3], they can also cause harm by oxidizing cellular components and molecules through the transfer of their unpaired electron [4], typically, free radicals are unstable and extremely reactive.

To counteract the damaging effects of free radicals, the body possesses its own internal antioxidant systems and also obtains antioxidants from the diet [5]. These antioxidants work to neutralize free radicals and maintain the body's overall balance, or homeostasis [6]. When there is an imbalance between free radicals and antioxidants, reactive oxygen species are produced; leading to oxidative stress [7], this oxidative stress has been linked to the development of various pathological conditions, including diabetes mellitus [8].

Reactive oxygen species (ROS) have been identified as substances that can disrupt enzymatic processes and contribute to various detrimental effects [9], such as lipid peroxidation [10], impaired Glutathione metabolism [11], and reduced levels of Vitamin C. In diabetes mellitus (DM) and hypertension, there are several biomarkers of oxidative stress that indicate the presence of this condition. These biomarkers include lipids, proteins, DNA damage, Glutathione, catalase, and superoxide dismutase [12, 13, 14].

Oxidative stress in patients with type 2 diabetes mellitus (T2DM) disrupts the balance of antioxidants within cells [15, 16], including enzymes like superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx) [17], and glutathione (GSH). Previous research has indicated that T2DM patients exhibit lower levels of total antioxidant status (TAS), GPx [18], and GSH compared to healthy individuals. GPx is an antioxidant enzyme that plays various roles, such as neutralizing lipid peroxides and hydrogen peroxide ( $H_2O_2$ ) [19, 20], eliminating reactive oxygen species (ROS), preventing the generation of new free radicals, and converting existing free radicals into less reactive molecules. The activity of GPx relies on GSH as both a direct scavenger and a co-substrate for the peroxidase enzyme. GSH serves as a primary buffer in the cellular reduction process against oxidation [22, 23]. GPx and GSH antioxidants are believed to provide beneficial effects in the body, including the prevention and repair of damage caused by free radicals [24, 25, 26, 27].

The objective of this research is to assess the extent of damage in diabetic patients with hypertension by examining their levels of Glycated hemoglobin, oxidative stress profile, and

lipid profile. Ultimately, this research aims to offer more information that will assist physicians in providing holistic interventions for the treatment and management of diabetes mellitus in patients attending JUTH (Jos University Teaching Hospital).

Diabetes mellitus is a metabolic disorder characterized by high blood glucose levels (hyperglycemia) and insufficient production or action of insulin in the body [28], which is produced by the pancreas [29]. Type 2 diabetes, also known as adult-onset diabetes, is a chronic disease that typically develops in middle- to late adulthood. However, it is increasingly being diagnosed in children and adolescents as well. Although type 2 diabetes is distinct from type 1 diabetes, they both share high blood sugar levels and the associated complications. There are currently 463 million adults living with diabetes globally. Without adequate measures to address this pandemic, the number is projected to reach 578 million by 2030 and a staggering 700 million by 2045 [30]. Diabetes mellitus is a significant global health burden, primarily due to persistent elevated blood glucose levels. Detecting and measuring oxidative stress biomarkers at an early stage can help predict and reduce the severity of these complications, thus slowing down the progression of the disease [31].

Type 2 diabetes and hypertension are two of the most prevalent factors contributing to cardiovascular disease (CVD). Many individuals with diabetes may not experience symptoms, and a significant portion (up to one-third) may be unaware of their condition. Hypertension, characterized by blood pressure higher than 140/90 mmHg, commonly coexists with diabetes, affecting 20-60% of diabetic patients depending on factors like ethnicity, age, and obesity [32]. In addition to cardiovascular complications, the presence of hypertension in diabetic patients increases the risk of end-stage renal disease and diabetic retinopathy. For patients with both hypertension and diabetes, aggressive pharmacological treatment to achieve blood pressure targets may be more crucial in reducing cardiovascular risk than controlling blood glucose levels. Due to the heightened risk of CVD in diabetic patients, stricter blood pressure targets are necessary. While tightly controlling blood glucose levels decreases the likelihood of microvascular complications like retinopathy and nephropathy, it has not been proven to reduce diabetes-related mortality or the occurrence of heart attacks (MI) [33].

Individuals with diabetes are at a heightened risk of developing serious and life-threatening complications, leading to increased healthcare needs, diminished quality of life, and added stress

on families [34]. Diabetes mellitus causes kidney damage, resulting in the retention of salt and water in the body, this, in turn, leads to an increase in blood pressure [35]. As diabetes progresses, it also damages the small blood vessels, causing them to become stiff and dysfunction [36], these alterations contribute to the development of elevated blood pressure [37].

## **2.0 Materials and Methods**

### **2.1 Data collection tool**

Informed consent Form

Questionnaire form

Interviews (structured interviews)

### **2.1 Administration of Questionnaire**

One on one interview was carried with the subject, which took about 20mins for each subject

### **2.3 Ethical Clearance**

Ethical approval for study was received from the Jos University Teaching Hospital Research Ethics Committee (approval N0 JUTH/DCS/IREC/127/2104). All relevant patients' clinical information was de-identified and anonymized

### **2.4 Study Area**

The study was out in Endocrinology Unit of Jos University Teaching Hospital (JUTH)

### **2.5 Blood collection and processing**

After administration of questionnaire to participants, 5mls of whole blood samples was collected from the antecubital vein, where 2.5mls was emptied into the EDTA bottle which was used to assay for HbA1c and Lipid profile while the remaining 2.5mls was emptied into the fluoride bottle which was further centrifuge at about 3500rpm using Centrifuge Universal 320R HETTICH for 5minutes to obtain the plasma and serum. When the centrifugation process was over, the serum was retracted using a pipette and delivered into a Z-5 bottle which was labeled then stored in a freezer at 90c Refrigerator (Haier thermocool: 518FR- 20 micropipettes) to stabilizing the proteins for further analysis.

### **2.6 Study design**

A Control case study was carried out on patient attending Medical Out-Patient Department (MOPD) Endocrinology Unit Clinic at JUTH, who were volunteers for the study, Questionnaire

was administered to patients followed by collection of their blood samples. Study participants were recruited into the study by their consultants, whose diabetic status was confirmed based on their several visits to the clinic.

The control group study was carried out among JUTH staffs that are not diabetic and were willing to volunteer for the study.

## **2.6.1 Inclusion and Exclusion criteria**

### **2.6.1.1 Inclusion Criteria**

1. Male and female aged 36 years to 70 years
2. Male and female patients with HbA1C confirmed diagnosis of Type 2 diabetes and the blood pressure was measured using a gauge, stethoscope and a blood pressure cuff
3. Confirmed Type 2 diabetes for not less than five years
4. Has been regular on the anti-diabetes medication
5. Written informed consent for study participation
6. NIDDM (Type II Diabetes Mellitus)

### **2.6.2.2 Exclusion Criteria**

1. Poorly controlled glucose level
2. History and documented evidence of systemic hypertension

## **2.9 Statistical Method Used (analysis)**

Data obtained for this study was entered into an Excel spreadsheet and then exported to the Statistical Package for Social Sciences (SPSS) version 25.0 for statistical analysis. Quantitative data was expressed as mean  $\pm$  standard deviation. A difference between means of the two groups was compared using Student's t-test. Chi-square test was used to determine association between categorical variables. A significance level of 0.05 and a confidence level of 95% was used for this study.  $P < 0.05$  was considered statistically significant.

## **2.10 Sample size determination**

The following formula for sample size determination was used to calculate the number of subjects recruited into the study

Using Sample size calculation for case control studies

$$n = \frac{Z^2 p(1-p)}{d^2}$$

Where n = sample size

Z = Standard normal variate for level of significance

d = Level of significance which is given by  $\alpha$

P = Prevalence

$$Z = 1.96$$

P = 0.036 (Prevalence in Jos metropolis)

$$1-P = 0.964$$

$$d = 0.05$$

$$z = 1.96 \text{ (constant)}$$

$p = 0.036$  (prevalence in Jos metropolis)

$$n = \frac{Z^2 p(1-p)}{d^2}$$

$$= \frac{(1.96)^2 0.036 \times 1 - 0.036}{(0.05)^2}$$

$$= \frac{3.86416 \times 0.036 \times 0.964}{0.0025}$$

$$= \frac{0.1341}{0.0025}$$

$$= 53 \cong 54$$

The determining of sample was divided into two groups Giving 27controls and 27 Test group [38]

### 3.0 RESULTS

The result obtained from this research work is analyzed to make comparison within and between both the test and control group.

#### 3.1 Demographic Characteristics of Study Participants

The Table below represents the result of demographic characteristics of the study participants. The mean age of the diabetic participants was  $55.85 \pm 8.07$  and that of control was  $41.80 \pm 9.05$  with a total mean age of  $50.50 \pm 10.93$ . 87.5% of the diabetics were above 50 years of age while in the control 80.0% were less than 50 years. With regard to gender, the diabetics were 50% each of male and female and the control group male constituted 30% and female accounted for 70%.

**Table 1. Demographic Characteristics of Study Participants**

Demographic characteristics	Diabetic	Control	Total
Mean age $\pm$ SD	$55.85 \pm 8.07$	$41.80 \pm 9.05$	$50.50 \pm 10.93$
<b>Age group (yrs)</b>			
<50	3(11.1)	21(77.8)	24(44.4)
$\geq$ 50	24(88.9)	6(22.2)	30(55.6)
<b>Gender</b>			
Male	13(48.1)	6(22.2)	19(35.2)
Female	14(51.9)	21(77.8)	35(64.8)

#### 3.2 Lifestyle of the Study Participants

The result of lifestyle of the respondents is as shown in table 5. The result shows that 81.5% of the diabetics exercise regularly while 50% did same in the control group. There was no significant difference ( $p=0.093$ ) between the two groups. Smoking status of the two groups shows that all (100%) of the two groups did not smoke. With regard to alcohol consumption, 100% each in the two groups did not consume alcohol. Majority (68.8%) of them in the diabetic group checked their blood sugar regularly as compared to 50% in the control, However, there was no significant difference ( $p=0.339$ ).

**Table 2. Lifestyle of the Study Participants**

Lifestyle	Diabetic	Control	$\chi^2$	p-value
<b>Do you exercise regularly?</b>				
Yes	22(81.5)	10(37.0)	11.045	0.001
No	5(18.5)	17(63.0)		
<b>Do you smoke?</b>				
Yes	0(0.0)	0(0.0)	-	-
No	27(100.0)	27(100.0)		
<b>Do you consume alcohol?</b>				
Yes	0(0.0)	0(0.0)	-	-
No	27(100.0)	27(100.0)		
<b>Do you check your blood sugar regularly?</b>				
Yes	21(77.8)	11(40.7)	7.670	0.006
No	6(22.2)	16(59.3)		

**3.3 Result of clinical assessment**

Result of clinical assessment of study participants is presented in table 6. The result indicates 18.5% of the diabetics were hospitalized while 81.5% were not and 100% of the control were not hospitalized. There was a significant difference in the diabetic group between those who were hospitalized and those who were not ( $p=0.014$ ). In the diabetic group, 77.8% attended session with a registered dietician with none (0.0%) in the control. The difference in the two groups was statistically significant ( $p=0.001$ ). Also 50% of the diabetics see endocrinologist or diabetes care physician on a regular basis and 50% did not while all (100%) in the control group did not as they were not diabetic.

**Table 3. Result of clinical assessment**

Variables	Diabetic	Control	$\chi^2$	p-value
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***Have you been hospitalized for your diabetes?***

Yes	5(18.5)	0(0.0)	5.510	0.019
No	22(81.5)	27(100.0)		

***Have you ever attended session with a registered dietician?***

Yes	21(77.8)	0(0.0)	34.364	0.001
No	6(22.2)	27(100.0)		

***Do you see your endocrinologist or diabetes care physician on a regular basis?***

Yes	14(51.9)	0(0.0)	18.900	0.001
No	13(48.1)	27(100.0)		

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**3.4 Comparison of oxidant, anti oxidant and HbA1C between diabetic and control among study participants**

Result of MDA, GSH, SOD, CAT and HbA1c obtained from the analysis, indicates that the mean MDA between diabetic and control groups among the study participants, indicates that the diabetic had  $1.78 \pm 0.82$  while control had  $1.13 \pm 0.08$ . The difference in the mean MDA between the two groups was statistically significant ( $p=0.001$ )

Mean GSH between diabetic and control as presented in table 6 shows that it was higher in the control having a mean value of  $10.47 \pm 2.04$  as compared with  $12.19 \pm 2.09$  for the diabetics. This difference was significant statistically ( $p=0.004$ ).

Mean SOD between diabetic and control as presented in table 4 shows that it was higher in the diabetic having a mean value of  $22.34 \pm 6.87$  when compared with  $13.94 \pm 1.78$  for control group. This difference was found to be statistically significant ( $p=0.001$ ).

The mean catalase between diabetic and control groups among the study participants. The diabetic had  $25.96 \pm 6.31$  and control had  $18.38 \pm 2.74$ . The mean catalase level was significantly higher in the diabetics than in the control ( $p=0.001$ )

Mean HbA1C between diabetic and control is as presented in table 4. The mean HbA1C level was higher in the diabetics having a mean value of  $9.17 \pm 2.68$  as compared with  $5.71 \pm 1.32$  for the control. The difference in mean HbA1C level between the two groups was statistically significant ( $p=0.001$ ).

**Table 4. Comparison of oxidant, anti oxidant and HbA1C between diabetic and control among study participants**

<b>Biomarkers</b>	<b>Diabetes Mean <math>\pm</math> SD</b>	<b>Control Mean <math>\pm</math> SD</b>	<b>t-test</b>	<b>p-value</b>
MDA	$1.78 \pm 0.82$	$1.13 \pm 0.08$	4.085	0.001
GSH	$10.47 \pm 2.04$	$12.19 \pm 2.09$	4.085	0.004
SOD	$22.34 \pm 6.87$	$13.94 \pm 1.78$	6.146	0.001
CATALASE	$25.96 \pm 6.31$	$18.38 \pm 2.74$	5.722	0.001
HbA1C	$9.17 \pm 2.68$	$5.71 \pm 1.32$	6.014	0.001

### **3.5 Comparison of MDA,GSH,SOD,CAT and HbA1C parameters between those who exercised within diabetic group**

Result of MDA, GSH,SOD, CAT and HbA1c between diabetic subjects who exercised and those that did not is as shown in table 6.

The analysis, indicates that the mean MDA for exercised diabetic was  $1.78 \pm 0.87$  while for non-exercised was  $1.77 \pm 0.63$ . The difference in the mean MDA between the two groups was not statistically significant ( $p=0.969$ )

Mean GSH between exercise diabetic and non exercised were  $10.47 \pm 1.83$  as compared with  $10.60 \pm 3.09$ . This difference was not significant statistically ( $p=0.880$ ).

Mean SOD for exercised diabetic was  $23.24 \pm 7.34$  when compared with  $18.38 \pm 0.46$  for non exercised diabetes. This difference was found to be statistically insignificant ( $p=0.158$ ).

The mean catalase between exercised diabetic was  $27.20 \pm 6.13$  and non diabetes had  $20.52 \pm 4.06$ . The mean catalase level was significantly higher in the diabetics that exercised than in the non exercised ( $p=0.030$ )

Mean HbA1C between exercised diabetic and unexercised diabetes were  $9.39 \pm 2.81$  and  $8.24 \pm 1.99$  respectively. Although the level is higher in exercised diabetes, however the difference was not statistically significant ( $p=0.399$ ).

**Table 5. Comparison of MDA,GSH,SOD,CAT and HbA1C parameters between those who exercised within diabetic group**

Parameter	Exercise		t-test	p-value
	Yes	No		
MDA	$1.78 \pm 0.87$	$1.77 \pm 0.63$	0.040	0.969
GSH	$10.44 \pm 1.83$	$10.60 \pm 3.09$	0.152	0.880
SOD	$23.24 \pm 7.34$	$18.38 \pm 0.46$	1.456	0.158
CATALASE	$27.20 \pm 6.13$	$20.52 \pm 4.06$	2.305	0.030
Hba1C	$9.39 \pm 2.81$	$8.24 \pm 1.99$	0.858	0.399

### 3.6 Comparison of lipid profile between diabetic and control among study Participants

Result of lipid profile between diabetic and control groups among the study participants is presented in table 5.

The mean TC for control was  $4.05 \pm 0.73$  and the diabetics group was  $5.13 \pm 1.02$ . There was statistically a significant difference between the two groups ( $p=0.001$ ).

The mean TG for control was  $1.75 \pm 0.95$  and that of diabetics group was  $1.44 \pm 0.88$  with no significant difference found between the two groups ( $p=0.227$ )

Mean LDL level showed that the control had  $1.86\pm 0.71$  while the diabetic group had  $2.74\pm 0.82$ . The diabetic group had a significantly higher mean LDL level when compared with the control group ( $p=0.001$ )

Mean value of HDL for control was  $1.33\pm 0.47$  while the diabetic group had  $1.79\pm 0.99$ . Also, the control group had a lower mean HDL level in relation to the diabetic group with ( $p=0.037$ )

**Table 6. Comparison of lipid profile between diabetic and control among study Participants**

Lipid profile	Control	Diabetics	t-test	p-value
TC	$4.05\pm 0.73$	$5.13\pm 1.02$	4.453	0.001
TG	$1.75\pm 0.95$	$1.44\pm 0.88$	1.224	0.227
LDL	$1.86\pm 0.71$	$2.74\pm 0.82$	4.206	0.001
HDL	$1.33\pm 0.47$	$1.79\pm 0.99$	2.144	0.037

### 3.7 Comparison of Lipid profile of those who exercised within diabetic group.

Result of diabetic subjects for those who exercised and those who did not exercise with respect to lipid profile is as presented in table 7.

The mean TC of diabetes who exercised was  $4.52\pm 0.13$  and those who did not was  $5.48\pm 1.15$ . There was statistically significant between the two groups ( $p=0.015$ ).

The mean TG for diabetes that exercise was  $1.22\pm 0.72$  and that of those who did not exercised was  $1.58\pm 0.97$  with no significant difference between the two groups ( $p=0.323$ )

Mean LDL level showed those who exercised had  $2.36\pm 0.41$  while those that did not exercised had  $2.96\pm 0.93$ . There was no significant difference between them ( $p=0.064$ )

Mean value of HDL for exercised diabetes patients was  $1.81\pm 0.50$  while those that did not exercised had  $1.77\pm 1.22$ . There was no significant difference between them ( $p=0.923$ )

**Table 7. Comparison of Lipid profile of those who exercised within diabetic group**

Parameter	Exercise		t-test	p-value
	Yes	No		

TC	4.52±0.13	5.48±1.15	2.626	0.015
TG	1.22±0.72	1.58±0.97	1.007	0.323
LDL	2.36±0.41	2.96±0.93	1.936	0.064
HDL	1.81±0.50	1.77±1.22	0.097	0.923

### 3.8 Parameters of Oxidant, Anti-oxidant and HbA1c who attended a session with a registered dietician within Diabetics (test group)

Result of MDA, GSH, SOD, CAT and HbA1c between diabetic study subjects who attended session with a registered dietician is presented in 10.

The result showed that mean MDA for diabetics that see dietician was 1.89±0.83 while those that do not see dietician was 1.41±0.73. No difference in the mean MDA between the two groups was not statistically significant (p=0.217)

Mean GSH between diabetics that see dietician and those who did not see dietician were 10.45±1.73 as compared with 10.54±3.12. There was no significant difference between means (p=0.927).

Mean SOD for diabetics that see dietician was 22.27±6.82 when compared with 22.59±7.74 for those that did not see dietician. This difference was found to be statistically insignificant (p=0.922).

The mean catalase between diabetics that see dietician was 28.26±5.17 and those that did not see dietician was 17.91±0.85. The mean catalase level was significantly higher in those that see dietician (p=0.001).

Mean HbA1C between diabetics that see dietician and those who did not were 9.64±2.55 and 7.55±2.72 respectively. The mean HbA1C level was not significantly difference (p=0.093)

**Table 8. Parameters of Oxidant, Anti-oxidant and HbA1c who attended a session with a registered dietician within Diabetics (test group)**

	Ever attended session with a registered Dietician	t-test	p-value
	Yes	No	

MDA	1.89±0.83	1.41±0.73	1.265	0.217
GSH	10.45±1.73	10.54±3.12	0.093	0.927
SOD	22.27±6.82	22.59±7.74	0.099	0.922
CATALASE	28.26±5.17	17.91±0.85	4.821	0.001
HbA1C	9.64±2.55	7.55±2.72	1.747	0.093

### 3.9 Lipid profile of Diabetics who attended a session with a registered dietician within Test Participants

Table 11 depicts the result of diabetics that see dietician and those who did not with regard to lipid profile.

The mean TC of diabetics who see dietician was 4.01±0.78 and those who did not was 4.22±0.55. There was a statistically significant difference between the two groups (p=0.036).

Mean TG for diabetics that see dietician was 1.80±1.08 and that those who did not see dietician was 1.58±0.20 with no significant difference between the two groups (p=0.325)

Mean LDL level showed those that see dietician had 1.76±0.73 while those that do not see dietician had 2.20±0.54. There was no significant difference between them (p=0.189)

Mean value of HDL for diabetics that see dietician was 1.33±0.53 while those that do not see dietician had 1.32±0.12. There was no significant difference between them (p=0.941)

**Table 9. Lipid profile of Diabetics who attended a session with a registered dietician within Test Participants**

Parameter	Ever attended session with a registered dietician		t-test	p-value
	Yes	No		
TC	4.01±0.78	4.22±0.55	0.619	0.541
TG	1.80±1.08	1.58±0.20	0.482	0.634
LDL	1.76±0.73	2.20±0.54	1.351	0.189
HDL	1.33±0.53	1.32±0.12	0.075	0.941

### 3.10 Comparison of oxidant, anti-oxidant and HbA1c Among the non-diabetics group who exercise

Table 10 depicts the result of MDA, GSH,SOD, CAT and HbA1c between control group who exercised and those that did not exercised.

The result, indicates that the mean MDA for exercised control group was  $1.13\pm 0.03$  while for non-exercised was  $1.14\pm 0.10$ . The difference in the mean MDA between the two groups was not statistically significant ( $p=0.829$ )

Mean GSH between exercise control groups and non exercised were  $10.90\pm 0.56$  as compared with  $12.96\pm 2.30$ . There was a significant difference between means of exercised and non exercised control group ( $p=0.011$ ).

Mean SOD for control group that exercised was  $14.49\pm 2.25$  when compared with  $13.62\pm 1.42$  for the non exercised. This difference was found to be statistically insignificant ( $p=0.230$ ).

The mean catalase between exercised control group was  $15.74\pm 1.52$  and non exercised control group was  $19.93\pm 2.20$ . The mean catalase level was significantly higher in the control group that did not exercised than in the exercised ( $p=0.001$ )

Mean HbA1C between exercised control group and unexercised were  $4.82\pm 0.27$  and  $6.24\pm 1.41$  respectively. The mean level is significantly higher in the non exercised control group ( $p=0.004$ )

**Table 10. Comparison of oxidant, anti-oxidant and HbA1c Among the non-diabetics group who exercise**

Parameter	Exercise		t-test	p-value
	Yes	No		
MDA	$1.13\pm 0.03$	$1.14\pm 0.10$	0.218	0.829
GSH	$10.90\pm 0.56$	$12.96\pm 2.30$	2.759	0.011
SOD	$14.49\pm 2.25$	$13.62\pm 1.42$	1.230	0.230
CATALASE	$15.74\pm 1.52$	$19.93\pm 2.20$	5.709	0.001
Hba1C	$4.82\pm 0.27$	$6.24\pm 1.41$	3.129	0.004

### 3.11 Lipid profile of non- diabetic who exercise among the control group

Result of the control study participants of those who exercised and those who do not exercise with respect to .lipid profile is as presented in table 9.

The mean TC of control who exercised was  $3.91\pm0.73$  and those who did not was  $4.66\pm0.35$ . There was a statistically significant between the two groups ( $p=0.036$ ).

Mean TG for control group that exercise was  $1.66\pm0.99$  and that those who did not exercised was  $2.14\pm0.79$  with no significant difference the two groups ( $p=0.325$ )

Mean LDL level showed those who exercised had  $1.71\pm0.70$  while those that do not exercised had  $2.52\pm0.29$ . There was significant difference between them ( $p=0.018$ )

Mean value for HDL of exercised control group was  $1.36\pm0.51$  while those that do not exercised had  $1.18\pm0.26$ . There was no significant difference between them ( $p=0.442$ )

**Table 11. Lipid profile of non- diabetic who exercise among the control group**

Parameter	Exercise		t-test	p-value
	Yes	No		
TC	$3.91\pm0.73$	$4.66\pm0.35$	2.212	0.036
TG	$1.66\pm0.99$	$2.14\pm0.79$	1.005	0.325
LDL	$1.71\pm0.70$	$2.52\pm0.29$	2.527	0.018
HDL	$1.36\pm0.51$	$1.18\pm0.26$	0.780	0.442

## 4.0 DISCUSSION AND CONCLUSION

### 4.1 Diabetics and Oxidative Stress

Diabetes poses significant health, economic, and societal burdens [39], and its prevalence is increasing globally due to factors like population growth, aging, urbanization, and rising obesity rates caused by physical inactivity [40]. Oxidative stress plays a critical role in the progression and development of diabetes and its complications, to mitigate the impact of oxidative stress and potentially reduce the occurrence of diabetes and its complications, interventions such as therapies, dietary plans, and behavioral changes can be beneficial. There is growing interest in the idea that uncontrolled lipid peroxidation [41,42], which is the result of reactive oxygen

species, is a major contributing factor in the development of coronary artery disease, particularly in Type II Diabetes [43]. Ultimately, lipid peroxidation is a series of injuries caused by free radicals [44], and the accumulation of free radical damage over time can lead to cell injury and the onset of various human diseases [45]. Free radicals have been implicated in the development of several diseases, including atherosclerosis, diabetes, hypertension, obesity, and cancer [46].

#### **4.2 Percentage of demographic, lifestyle and clinical analysis**

Table 1 presents the result of demographic characteristics of the study participants. The mean age of the diabetic participants was  $55.94 \pm 8.24$  and that of control was  $41.80 \pm 9.05$  with a total mean age of  $50.50 \pm 10.93$ . Further, 87.5% of the diabetics were above 50 years of age while in the control 80.0% were less than 50 years. With regard to gender, the diabetics were 50% each of male and female and the control group male constituted 30% and female accounted for 70%.

Table 2 displays the lifestyle habits of the respondents. The results indicate that 81.3% of individuals with diabetes engage in regular exercise, while 50% of the control group does the same. Regular physical exercise alone can have a positive impact on managing diabetes mellitus [47]. Moderate exercise leads to a tenfold increase in fat oxidation due to elevated energy expenditure and greater availability of fatty acids. This increased fatty acid availability stems from both heightened lipolysis and reduced re-esterification of Non-esterified Fatty Acid (NEFA) into triglycerides [48]. The use of  $\beta$ -blockade during exercise suppresses lipolytic activity, thereby decreasing NEFA levels. Physical exercise has been reported to enhance insulin sensitivity and improve glucose metabolism [49]. Diabetic patients who frequently exercise (table 7) experience changes in their lipid profile and reduced levels of reactive oxygen species [50]. Continuous exercise-induced improvements in biochemical parameters can alleviate complications associated with diabetes, including neuropathy, retinopathy, and nephropathy [51]. There was no significant difference ( $p=0.093$ ) between the two groups (table 3), smoking status of the two groups shows that all (100%) of the two groups did not smoke. With regard to alcohol consumption, 100% each in the two groups did not consume alcohol. Majority (68.8%) of them in the diabetic group checked their blood sugar regularly as compared to 50% in the control, however, there was no significant difference ( $p=0.339$ ).

Result of clinical assessment of study participants is presented in table 3 indicates 18.8% of the diabetics were hospitalized while 81.3% were not and 100% of the control were not hospitalized.

However, There was a significant difference in the diabetic group between those who were hospitalized and those who were not ( $p=0.014$ ). In the diabetic group (table 3), 68.8% attended session with a registered dietician with none (0.0%) in the control, the difference in the two groups was statistically significant ( $p=0.001$ ). Also 50% of the diabetics see endocrinologist or diabetes care physician on a regular basis and 50% did not while all (100%) in the control group did not as they were not diabetic. From the clinical assessment it shows (table 3) that diabetes mellitus patients who are on regular visit to the endocrinologist stand a better chance of living a healthy life style than those who did not.

#### **4.3 Percentage of Oxidative stress biomarkers and HbA1c**

MDA (malondialdehyde) has been identified as a primary biomarker of lipid damage and oxidative stress caused by free radicals [52]. Diabetes, particularly in patients with vascular complications, is associated with significant changes in lipid metabolism and structure [53]. The elevated levels of MDA observed in diabetic individuals suggest that oxidative damage may contribute to the development of diabetic complications [54]. The increase in lipid peroxidation also indicates a decline in the protective mechanisms provided by enzymatic and nonenzymatic antioxidants [55]. MDA is produced as a decomposition product of oxidized lipids [56, 57], and this process is believed to involve the formation of prostaglandins (such as endoperoxides) from polyunsaturated fatty acids (PUFAs) with two or more double bonds. Several studies have reported increased levels of MDA in plasma, serum, and various tissues of diabetic patients [58, 59] which align with the findings of this study. Comparing mean levels MDA between diabetic and control groups among the study participants, the diabetic had  $1.78\pm 0.82$  while control had  $1.13\pm 0.08$ , the difference in the mean MDA between the two groups was statistically significant with ( $p=0.001$ ). There was an increased levels of MDA in the diabetic group as compared to the control, the increase observed may be due to exposure and increased levels of hyperglycemia which has been indicated by the HbA1c and lipid profile (table 4 and 6 respectively). Increased level of MDA in diabetics suggests that peroxidative injury may be involved in the development of diabetic complications [60]. The increase in lipid peroxidation is also an indication of decline in defence mechanisms of enzymatic and nonenzymatic antioxidants [61]. There has been considerable interest in the concept that the uncontrolled lipid peroxidation is a key contributing factor in the pathophysiology of CAD especially in Type II Diabetes [62]. Lipid peroxidation eventually is a sequence of the injury caused by ROS [63]. Similar results have been reported in

type II DM patients [64, 65]. Free radical damages can accumulate over time and may thereby contribute to cell injury and development of human diseases [66]

GSH can maintain SH groups of proteins in a reduced state [67], they participate in amino acid transport, detoxify foreign radicals, act as coenzyme in several enzymatic reactions, and also prevent tissue damage. It is an efficient antioxidant present in almost all living cells and is also considered as a biomarker of redox imbalance at cellular level [68]. There are several reports that claim a reduced level of GSH in diabetes [69]. Decreased GSH level may be one of the factors in the oxidative DNA damage in type 2 diabetics [70, 71]. The result (table 4) for GSH shows that there was a decrease level of GSH in the diabetic group as compared to the control, Mean GSH between diabetic and control as presented shows that it was higher in the control having a mean value of  $10.47 \pm 2.04$  as compared with  $12.19 \pm 2.09$  for the diabetic which was lower, this difference was significant statistically having a P ( $p=0.004$ ). This study is in agreement with other study which showed a decrease in the reduced GSH level has been reported in the erythrocyte of diabetics [72]. Decrease in the level of GSH occurs both due to the competition between aldose reductase and glutathione reductase for NADPH, a cofactor, and increased oxidative stress (increased ratio of NADH/NAD [73]. These data suggest that the oxidative stress in these pathologies does not depend on a loss of GSH or a lack of GSH synthesis alone, but a misbalance in the oxidant/reduction cycle of GSH [74, 75]

Superoxide dismutase (SOD) is the antioxidant enzyme that catalyses the dismutation of superoxide anion ( $O_2^-$ ) into hydrogen peroxide and molecular oxygen [76]. SOD plays important protective roles against cellular and histological damages that are produced by ROS [77]. It facilitates the conversion of superoxide radicals into hydrogen peroxide, and in the presence of other enzymes it converted into oxygen and water [78]. The elevated level of SOD is shown to reduce oxidative stress [79]; decrease mitochondrial release of cytochrome C and apoptosis in neurons; and, in mice, prevent diabetes-induced glomerular injury, thus suggesting a major role of SOD in the regulation of apoptosis [80]. Decline in the level of SOD in diabetic tissue and blood has been reported in many studies [81, 82]. Mean SOD between diabetic and control as presented in table 4 shows that there was an increased levels in the diabetic group having a mean value of  $22.34 \pm 6.87$  in the diabetics when compared with  $13.94 \pm 1.78$  for control group having a p value of  $p = 0.001$ . The increase in SOD activity could be due to its induction

by increased production of superoxide [83]. To sum it up, the activities of SOD an enzymatic oxidant significantly increased in the diabetic patients as compared to the control test group. In a similar study carried out [84, 85] the total SOD activity and the lipid peroxidation were higher in diabetics compared to nondiabetics. In stratified groups, the total SOD activity was different for the hypertensive diabetics compared to the prediabetics and normotensive controls. Lipid peroxidation was significantly higher in both groups of diabetics (hypertensive and normotensive) compared to prediabetic groups and hypertensive and normotensive controls [86].

Catalase is an antioxidative enzyme present nearly in all living organisms; it plays an important role against oxidative stress-generated complications such as diabetes and cardiovascular diseases [87]. Catalase acts as main regulator of hydrogen peroxide metabolism, hydrogen peroxide is a highly reactive small molecule formed as natural by-product of energy metabolism. Prevalence of oxidative stress is reported in all processes where reduced/depleted plasma antioxidant potential is reported including aging and hypertension. Increased oxidative damage as well as reduction in antioxidant capacity could be related to the complications in patients with type 2 diabetes [88]. Mean catalase between diabetic and control groups among this study participants showed that the diabetic had  $25.96 \pm 6.31$  and control had  $18.38 \pm 2.74$ . The mean catalase level was statistically significantly higher in the diabetics than in the control having a ( $p=0.001$ ). Increased oxidative stress as well as reduction in antioxidant capacity could be related to the complications in patients with diabetes such as oxidative DNA damage and insulin resistance, due to decrease in antioxidant potential of plasma, complications of diabetes increases which include cardiovascular disease, nerve damage, blindness, and nephropathy. Thus, the increasing incidence of diabetes is a significant health concern beyond the disease itself [89]. Catalase enzymatically processes hydrogen peroxide into oxygen and water and thus neutralizes it, also, increased risk of diabetes has been documented in patients with catalase deficiency [90]. The deficiency of this enzyme leads to an increase in oxidative stress and ultimately to a failure  $\beta$ -cell type.  $\beta$ -cells are rich in mitochondria, and thus their organelles might be a source of ROS [91]. In this study there was a significant increase of catalase in the diabetic group as compared with the control group.

Glycated hemoglobin (HbA1c) level reflects the mean glucose concentration over last 8-12 weeks approximately and provides a much better indication of long-term glycemic control [92].

Mean HbA1C between diabetic and control is as presented in Table 4. The mean HbA1C level was higher in the diabetics having a mean value of  $9.17 \pm 2.68$  as compared with  $5.71 \pm 13.2$  for the control. The difference in mean HbA1C level between the two groups was statistically significant ( $p=0.001$ ). Other studies have shown that glycated hemoglobin (HbA1c) was higher in diabetics compared to pre-DM and the controls [93, 94].

### **5.3 Percentage of Lipid profile**

Diabetes is characterized by high blood sugar levels and changes in glucose and lipid metabolism [95]. These changes can lead to damage in cell membranes, resulting in increased production of reactive oxygen species (ROS). The elevated levels of ROS and decreased antioxidant defense mechanisms in diabetic patients may contribute to the development of complications. To reduce the risk of complications such as blindness, kidney failure, and limb amputation, it is necessary to control not only blood glucose levels but also lipid levels [96]. In diabetes, high blood glucose levels are often accompanied by increased levels of plasma cholesterol, triglycerides, LDL, and VLDL, as well as decreased levels of HDL [97]. Table 6 shows a statistically significant difference between diabetics and non-diabetics, which is consistent with other studies [98]. Non-diabetics had significantly lower levels of total cholesterol and LDL compared to diabetics, while their HDL levels were significantly higher [99].

Cholesterol is transported in the blood by proteins called lipoproteins. There are two types of lipoproteins: LDL (low-density lipoprotein), often referred to as "bad" cholesterol, and HDL (high-density lipoprotein), known as "good" cholesterol. LDL cholesterol contributes to the buildup of plaque on the walls of blood vessels, leading to narrowed arteries and increased risk of heart disease and stroke. On the other hand, HDL cholesterol helps remove cholesterol from the bloodstream and reduces the risk of heart disease and stroke [100, 101].

When there is an excess of LDL cholesterol, it can accumulate as plaque [102], causing the narrowing of blood vessels over time. This narrowing restricts blood flow to the heart and other organs [103]. It has been proposed that the increase in triglyceride levels in diabetes may be attributed to insulin deficiency, which impairs glucose utilization and leads to hyperglycemia. In response, fatty acids are mobilized from adipose tissue for energy purposes [104]. However, excess fatty acids can accumulate in the liver and be converted into triglycerides. Insulin plays a role in increasing the number of LDL receptors, so chronic insulin deficiency may result in

reduced levels of LDL receptors. This leads to an increase in LDL particles and subsequently elevated LDL cholesterol levels in diabetes mellitus [105].

High levels of cholesterol, triglycerides, LDL cholesterol, and low levels of HDL cholesterol in diabetes may be attributed to factors such as obesity, increased calorie intake, and lack of physical exercise. This research (as shown in table 7) indicates that regular exercise can reduce the risk of high LDL and total cholesterol levels among diabetic patients at JUTH. Diabetics who engaged in regular exercise had lower LDL and total cholesterol levels compared to those who did not exercise. The findings suggest that exercise is crucial in the prevention of various diseases, including diabetes and its complications. Table 11 also demonstrated that healthy non-diabetic individuals who regularly exercised had lower LDL and total cholesterol levels compared to those who did not exercise. Additionally, those who frequently exercised had higher levels of HDL cholesterol, which is considered beneficial. The research presented in tables 8 and 9 further highlights the significance of visits to dietitians and clinicians and dietary changes in reducing the risk of diabetes and its complications.

Assessing lipid peroxide levels along with other lipid profiles in diabetes mellitus can serve as a useful indicator for monitoring the prognosis of patients [106]. Detecting risk factors in the early stages of the disease can assist patients in improving their condition and reducing morbidity rates.

#### **5.4 Conclusion**

Regardless of whether someone is diabetic or not, engaging in regular exercise and following a healthy diet plan is highly recommended for everyone. These lifestyle factors are particularly important for individuals with diabetes as they can contribute to better glycemic control, weight management, and overall well-being. Exercise helps improve insulin sensitivity, promotes cardiovascular health, and aids in weight management. A balanced and nutritious diet, rich in fruits, vegetables, whole grains, lean proteins, and healthy fats, provides essential nutrients and helps maintain stable blood sugar levels.

Glycemic control is a crucial factor in the development of oxidative stress and the subsequent risk of long-term complications in diabetes [107]. The findings of this study suggest that individuals with good glycemic control experience lower levels of oxidative stress compared to

those with poor glycemic control. Improved glycemic control reduces hyperglycemia, which in turn reduces the influx of glucose into pathways such as the polyol pathway and other shared metabolic pathways associated with comorbidities. This leads to an increase in NADH concentration and the activity of the antioxidant enzyme glutathione peroxidase. Reduced oxidative stress also decreases the glycation and inactivation of superoxide dismutase. Therefore, maintaining good glycemic control plays a crucial role in the prevention of diabetes complications. In diabetic conditions, the activities of the reduced glutathione oxidative enzyme system are found to be low, while those of catalase and superoxide dismutase are increased. Additionally, achieving fair glycemic control reduces lipid peroxidation and improves the antioxidant defense system. Therefore, the management of diabetes should also focus on dietary management of antioxidants and other phytochemicals to reduce oxidative stress and delay the onset of complications.

Estimating lipid peroxide levels, along with other lipid profiles, in individuals with diabetes mellitus can be a useful tool for monitoring and assessing the prognosis of patients. Detecting risk factors in the early stages of the disease can help patients improve their condition and reduce the morbidity rate. Barriers to achieving good glycemic control include limited access to quality healthcare, lack of awareness among patients and healthcare providers, and concerns about potential side effects of tight control, especially among older and frail individuals. Furthermore, conducting more studies to gather additional statistical data is essential in addressing the challenges and complications associated with diabetes. Research plays a crucial role in expanding our understanding of the disease, identifying risk factors, developing effective interventions, and improving overall management strategies. By obtaining more comprehensive data, we can enhance prevention, diagnosis, and treatment approaches, ultimately reducing the impact of diabetes and its complications on individuals and society as a whole.

### **5.5 Recommendation**

Early detection and intervention are crucial in reducing the complications associated with oxidative stress in type 2 diabetes. Once a diagnosis is made and patients are found to have hyperglycemia, assessing their lipid peroxidation and antioxidant parameters can help identify individuals at risk for complications related to diabetes. By monitoring these parameters,

healthcare providers can intervene early and implement appropriate strategies to manage oxidative stress, thereby reducing the likelihood of complications in diabetes.

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