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1 *Original Research Article*
2
3 # CORRELATION BETWEEN OXIDATIVE STRESS MARKERS AND ATHEROGENIC INDICES
4 IN TYPE 2 DIABETES MELLITUS
5
6 ## ABSTRACT

7 Worldwide, approximately 200 million individuals are currently suffering of type 2 diabetes mellitus (DM).
8 Diabetes mellitus is associated with hyperglycemia, which induces oxidative stress that is responsible for
9 the various complications associated with the disease. This study was designed to know the relationship
10 between oxidative stress and atherogenic indices of plasma in type 2 diabetic and non-diabetic subjects.
11 A total number of eighty (80) subjects comprising 58 diabetic subjects with mean age (62.91±10.57) years
12 and 22 non-diabetic subjects with mean age (55.27±16.62) years were studied. Estimation of enzymatic
13 and non-enzymatic oxidative stress markers (which include MDA, SOD, GPx, CAT, Uric acid and
14 Albumin) and atherogenic indices (TCHOL, TG, HDL, LDL) were done respectively using standard
15 spectrophotometric techniques. The plasma mean of SOD, GPx, CAT and albumin were significantly
16 lower in diabetic subjects compared with control group. However, TChol, HDL, MDA and uric acid were
17 significantly higher in diabetic subjects compared with controls. The findings of this study show significant
18 differences in dyslipidemia, lipid peroxidation and increasing of oxidative stress markers from naïve type 2
19 diabetic subjects through controls. Thus, early diagnosis and management of this condition is necessary
20 in order to incorporate antioxidant supplement as a supportive therapy for adequate glycaemic control.

21 **Keywords:** Diabetes mellitus, Oxidative stress, antioxodant, CVD, atherogenic indices
22

23 1.0 INTRODUCTION

24 Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases characterized
25 by chronic hyperglycaemia over a prolonged period. Diabetes is either due to the pancreas inability to
26 produce adequate insulin or insulin resistant to the cells of the body [1]. As of 2014, estimated 387 million
27 diabetes cases have been reported worldwide [2] with type 2 DM making up about 90% of the case [3].

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28 This represents 8.3% of the adult population with equal rates in both women and men [4]. From 2012 to
29 2014, diabetes is estimated to have resulted in 1.5 to 4.9 million deaths each year and the number of
30 individuals with diabetes are expected to rise to 592 million by 2035 [5]. Diabetes has been reported to at
31 least double individuals' risk of death [6].
32 There are three main types of diabetes mellitus as reported by Picot *et al.* [7]: Type 1 DM, type 2 DM and
33 gestational diabetes. Inability of the pancreas to produce enough insulin is the main cause of type 1 DM
34 and this type was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile
35 diabetes" [4]. Type 2 DM begins with insulin resistance; a condition in which cells fail to respond to insulin
36 properly [4]. As the disease progresses, a lack of insulin may also develop [8]. This form was previously
37 referred to as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The primary
38 cause is excessive body weight and inadequate exercise [4]. Gestational diabetes is the third main type
39 and occurs when pregnant women without a previous history of diabetes develop hyperglycaemic
40 condition [4]. Type 2 diabetes is typically a chronic disease associated with a ten-year-shorter life
41 expectancy. Long-term complications from this condition includes heart disease, strokes, diabetic
42 retinopathy, kidney failure, and poor blood flow in the limbs leading to amputations [1].
43 Free radicals are atoms or group of atoms with an unpaired number of electron(s) in their outer most shell
44 and can be possibly formed when oxygen interacts with certain biomolecules [9]. Once formed, these
45 highly reactive species can start a chain reaction. Their chief danger comes from the damage they can do
46 when they react with important cellular component such as DNA, or the cell membrane [9]. Cells might
47 function poorly or die if this eventually occurs and could not be arrested on time. To prevent free radical
48 effect(s), the body has a defense mechanism system of antioxidant [10]. An antioxidant is a molecule that
49 inhibits the oxidation of other molecules, while oxidation is a chemical reaction that can produce free
50 radicals, leading to chain reaction that may damage cells. Thus antioxidant such as thiols or ascorbic
51 acid terminates this chain reaction [11]. To balance the oxidative state, plant and animal maintain
52 complex system of overlapping antioxidant, such as glutathione and enzymes (such as catalase)
53 produced internally or Vitamin C, Vitamin A, and Vitamin E obtained by ingestion [12]. Antioxidants are
54 widely used in dietary supplements and have been investigated to be highly effective for the prevention of
55 diseases such as cancer and coronary heart diseases [13].

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56 Oxidative stress reflects an imbalance between the systemic manifestation of reactive oxygen species
57 (ROS) and a biological system's ability to readily detoxify the reactive intermediates or to repair the
58 resulting damage. Disturbances in the normal redox state of cells could possibly cause toxic effects
59 through the production of peroxides and free radicals that damage body's biomolecules, including
60 proteins, lipids, and DNA [14]. Oxidative stress from oxidative metabolism has been reported to cause
61 base damage, as well as break strand in DNA [15]. In humans, oxidative stress is thought to be involved
62 in the development of atherosclerosis and had been sited to be of etiological importance in cardiovascular
63 diseases [16], which could be related to diet and also metabolic disorders with abnormal lipid metabolism
64 [17]. In either of the case it results to atherosclerotic endothelial dysfunction from arterial diseases and
65 this has been reported to be responsible for about 30% of death worldwide [16]. Diabetes mellitus is
66 characterized with hyperglycemia, which may induce oxidative stress that is responsible for the various
67 complications associated with the disease [18], which affects the heart, the nerves and the retina resulting
68 into heart disorders [19]. The characteristics of diabetic mellitus such as hyperglycemia, dyslipidemia,
69 inflammation and oxidative stress affect the vascular wall and thus accelerate atherosclerosis and its
70 clinical complications [10]. Atheroslerotic disorder of the coronary arteries usually result in partial or
71 complete occlusion of vascular lumen and this is of pathologic significance in determining the morbidity
72 and mortality pattern of ischemic heart disease (IHD) [10]. Coronary artery disease (CAD) is initially
73 symptomless with normal basic activities but as the disease progresses, the degree of lumen narrowing is
74 sufficiently great and this limit increase in blood flow during exercise and thus producing symptoms of
75 angina pectoris which can lead to heart attack [20].

76 Oxidative stress is associated with increased production of oxidizing species or a significant decrease in
77 the effectiveness of antioxidant defenses, such as glutathione [21]. The effects of oxidative stress depend
78 upon the size of these changes, with a cell being able to overcome small perturbations and regain its
79 original state. However, more severe oxidative stress can cause cell death and even moderate oxidation
80 can trigger apoptosis, while more intense stress may cause necrosis [22]. Worldwide, approximately 200
81 million individuals are currently suffering of type 2 diabetes mellitus (DM) [2]. Some studies have shown
82 that Type 2 DM subjects generally carry a number of risk factors for coronary vascular disease (CVD),

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83 which is found to be characterized with hyperglycemia, abnormal lipid profiles pattern and alterations in
84 inflammatory mediators [20]. Thus, diabetes mellitus associated with cardiovascular diseases tends to be
85 one of the highest causes of death worldwide. This study therefore aimed to know the relationship
86 between oxidative stress biomarkers and atherogenic indices of plasma in type 2 diabetes mellitus, which
87 might contribute to the incidence of CVD in this condition if it is not ameliorated on time.

88 2.0 MATERIALS AND METHODS

89 2.1 Study population

90 This study was conducted at Federal Medical Centre, Owo, Ondo State. Owo is a town in Ondo State
91 situated at south-western Nigeria, with latitude 710’59.998’’N and longitude 534’59.988’’E at an average
92 altitude of 348 meters. It is at the southern edge of the Yoruba hills, and at the intersections of roads from
93 Akure and Benin City. The community has a population of 276, 593 according to national population in
94 the year 2006 census [23].

95 2.2 Study design

96 This is a case-control study and it was conducted at Federal Medical Centre, (FMC) Owo, which serve as
97 tertiary health institutions in Ondo State. The research was conducted between January to July, 2016. A
98 total number of eighty (80) type 2 diabetes mellitus subjects (both males and females) aged between 30 –
99 80 years, which were sub-divided into diabetic mellitus subjects under treatment, DMUT and naïve
100 diabetic subjects (which are newly diagnosed type 2 diabetes mellitus) attending diabetic clinic at Federal
101 Medical Centre, Owo were randomly selected for this study. Type 2 diabetes mellitus subjects in this
102 study were diagnosed according to guideline of WHO [24]. Their medical history and personal data was
103 obtained via short structured questionnaire after due approval from the ethical committee of the hospital.
104 Forty (22) age and sex matched apparently healthy controls with no history of diabetes mellitus were
105 enrolled into this study. Informed consent was thus obtained from all the participants.

106 2.3 Ethical clearance and consent

107 Subjects participating in this study were fully briefed on the research protocols in the clinic after which
108 they were being required to sign a written consent. After that, a pre-designed structural questionnaire was

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109 utilized to collect bio-data, and socio-demographic characteristics of the patients. Approval for this study
110 was obtained from the Federal Medical Centre, Owo and Ethical Clearance
111 (FMC/OW/380/VOL.XXIX/197) was issued by Ethical Committee Federal Medical Centre, Owo.

112 **2.4 Collection and Storage of Samples**

113 Blood samples were obtained from each subject by applying a tourniquet around the arm above elbow.
114 The ante-cubital forsa was disinfected with a 70% alcohol soaked swab. Six milliliters (6mls) of venous
115 blood was collected from each subject using aseptic procedure after 12 hours fast. 4mls of venous blood
116 was dispensed into 5 ml sterile vacutainer bottle containing lithium heparin anticoagulant and gently
117 mixed by inverting the container severally for the determination of lipids profile and oxidative stress
118 markers. The remaining (2mls) of the venous blood was dispensed into 3mls vacutainer bottle containing
119 fluoride oxalate anticoagulant which was also mixed gently by inverting the container several times for the
120 determination of plasma glucose. Plasma was separated from the blood by centrifugation for 5 minutes at
121 4000rpm, into plain bottles and stored at -20℃ until time of analysis.

122 **2.5 Analytical Methods**

123 Height (m) was taken using a Stadiometer while body weight (kg) was taken using a body weight
124 weighing scale with the subject wearing light clothing and without shoes. Body mass Index (BMI) was
125 calculated as the ratio of weight (kg) to the square of height (m^2). Blood pressure and pulse rate were
126 taken simultaneously using a sphygmomanometer. Blood levels of fasting blood sugar and lipids profile
127 were determined using standard spectrophotometric method [25] and standard methods were employed
128 for the determination of SOD, CAT and GPx plasma activities [26, 27] and plasma levels of MDA, Uric
129 acid and albumin [28, 29, 30].

130 **2.6 Statistical analysis of data**

131 A statistical package for social scientist (SPSS) 17.0 was used for the analysis of the data appropriately.
132 Continuous variables were displayed as means and standard deviation (SD) and categorical variables
133 were displayed as percentage. The level of significance was taken at 95% confidence interval and P
134 value less than 0.05 was considered significant.

135 **3.0 RESULTS AND DISCUSSION**

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136 **3.1 Results**

137 A total number of eighty (80) subjects comprising 58 diabetic subjects with mean age (62.91±10.57) years
138 and 22 non-diabetic subjects (control) with mean age (55.27±16.62) years were studied. Twenty three
139 (23) out of the diabetic subjects were naïve (i.e. not yet placed on diabetic drugs) while the remaining 35
140 were already undergoing treatment.

141 Table 1 shows the age and sex distribution of all participants. Participants were aged between 30 and 80
142 years. There were 34 females and 24 males, and 13 females and 9 males in diabetic and non-diabetic
143 groups respectively. Thus, females constituted 58.75% while males constituted 41.25% in overall.

144 Table 2 shows anthropometric indices and biochemical parameters in both diabetic and non-diabetic
145 subject population. The mean body mass index (BMI), pulse, systolic blood pressure (SBP) and diastolic
146 blood pressure (DBP) were significantly higher in diabetic subjects compared with controls, while there
147 were no statistical significant in mean height and weight. The mean SOD, GPx, CAT and albumin were
148 significantly lower in diabetic subjects compared with control group. However, TChol, HDL, MDA and uric
149 acid were significantly higher in diabetic subjects compared with controls.

150 Table 3 shows the anthropometric indices and biochemical parameters in diabetic subjects (naive and
151 under treatment) and controls using One way analysis of variance (ANOVA), the mean BMI. Pulse, SBP,
152 DBP, FBS, TChl, TAG, HDL, MDA, Uric acid, SOD, GPx and CAT were significantly different among the
153 three groups

154 Table 4 indicates correlation of plasma levels of enzymatic antioxidant biomarkers with atherogenic
155 indices and other parameters in diabetic subjects. CAT had positive correlation with FBS, TChol, TAG
156 and LDL, but inverse correlation with HDL. Also, SOD showed statistical negative correlation with TChol,
157 TAG, HDL and LDL, while GPx only had positive correlation with HDL, TChol:HDL and LDL:HDL. Finally,
158 table 5 shows plasma levels of MDA had significant positive correlation with FBS, TChl and LDL. Uric acid
159 showed statistical positive significant correlation with blood pressure (SBP and DBP), while albumin only
160 had significant inverse correlation with pulse.

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163 **Table 1: Age and Sex distribution of the Subject population in percentage (%)**

Age group (Years)	Diabetic Subjects		Non-diabetic subjects		Total
	Male	Female	Male	Female	
31-40	-	1 (1.25)	4 (5)	3 (2.75)	8 (10)
41-50	8 (10)	2 (2.5)	-	3 (3.75)	13 (16.25)
51-60	2 (2.5)	8 (10)	1 (1.25)	2 (2.5)	13 (16.25)
61-70	10 (12.5)	15 (18.75)	1 (1.25)	3 (2.75)	29 (36.25)
71-80	4 (5)	8 (10)	3 (3.75)	2 (2.5)	17 (21.25)
Total	24 (30)	34 (42.5)	9 (11.25)	13 (16.25)	80 (100)

164

165 **Table 2: anthropometric indices and biochemical parameters in both diabetic and non-**

166 **diabetic subject population**

167

Parameters	Diabetic subjects (n=58)	Non-diabetic subjects (n=22)	P-value
BMI (Kg/m^2)	28.93±7.68	24.88±5.11	0.025*
Pulse (b/m)	74.71±5.09	69.09±3.04	0.000*
SBP (mmHg)	129.16±13.25	115.73±8.69	0.000*
DBP (mmHg)	83.10±7.66	75.64±5.38	0.000*
FBS (mmol/l)	10.47±4.77	4.57±0.61	0.000*
TChl (mmol/l)	5.04±1.35	4.26±1.01	0.016*
TAG (mmol/l)	1.80±0.79	1.46±0.74	0.083
HDL (mmol/l)	1.42±0.47	1.04±0.27	0.001*
LDL (mmol/l)	2.81±0.91	2.56±0.62	0.252
TChl:HDL	3.80±1.34	4.20±0.74	0.186
LDL:HDL	2.19±1.08	2.57±0.68	0.127
SOD (U/ml)	2.03±0.69	3.19±1.39	0.000*
MDA (µmol/l)	3.25±1.45	2.51±0.96	0.030*
GPx (U/ml)	2.03±0.75	2.90±0.90	0.000*

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CAT (U/L)	20.65±6.57	27.91±6.87	0.000*
Uric Acid (mmol/l)	392.71±174.54	287.99±125.75	0.012*
Albumin (mg/dl)	36.45±5.55	38.39±4.10	0.140

168 * significant at $p<0.05$

169 **Table 3: Anthropometric indices and biochemical parameters in diabetic subjects (naive**
170 **and under treatment) and controls**
171

Parameters	Naïve DM (n=23)	DMUT (n=35)	Control (n=22)	F-value
BMI (Kg/m^2)	30.44±6.28	27.94±8.42	24.88±5.11	0.035*
Pulse (b/m)	78.04±4.65	72.51±4.13	69.09±3.04	0.000*
SBP (mmHg)	135.00±12.61	125.31±12.38	115.73±8.69	0.000*
DBP (mmHg)	85.43±7.22	81.57±7.65	75.64±5.38	0.000*
FBS (mmol/l)	13.50±4.95	8.47±3.45	4.57±0.61	0.000*
TChl (mmol/l)	5.38±1.37	4.82±1.31	4.26±1.01	0.015*
TAG (mmol/l)	2.21±0.86	1.53±0.62	1.46±0.74	0.001*
HDL (mmol/l)	1.44±0.38	1.40±0.53	1.04±0.27	0.003*
LDL (mmol/l)	2.93±0.93	2.72±0.90	2.56±0.62	0.342
TChl:HDL	3.95±1.64	3.70±1.12	4.20±0.74	0.310
LDL:HDL	2.21±1.29	2.18±0.94	2.57±0.68	0.312
SOD (U/ml)	2.12±0.47	1.96±0.81	3.19±1.39	0.000*
MDA (µmol/l)	3.44±1.07	3.12±1.66	2.51±0.96	0.065
GPx (U/ml)	2.10±0.68	1.99±0.79	2.90±0.90	0.000*
CAT (U/L)	19.76±5.71	21.23±7.11	27.91±6.87	0.000*
Uric Acid (mmol/l)	437.30±155.11	363.41±182.41	287.99±125.75	0.010*
Albumin (mg/dl)	33.56±5.07	38.35±5.07	38.39±4.10	0.001*

172 * significant at $p<0.05$
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176 **Table 4: Correlation of plasma levels of enzymatic antioxidant biomarkers with**
177 **atherogenic indices and other parameters in diabetic subjects**

	SOD		GPx		CAT	
	r-value	p-value	r-value	p-value	r-value	p-value
BMI (Kg/m^2)	-0.151	0.259	0.040	0.765	-0.096	0.474
Pulse (b/m)	0.130	0.332	0.108	0.419	0.015	0.910
SBP (mmHg)	-0.033	0.807	-0.063	0.638	- 0.159	0.234
DBP (mmHg)	-0.112	0.404	-0.127	0.342	-0.253	0.056
FBS (mmol/l)	-0.064	0.635	-0.250	0.059	-0.373	0.004*
TChl (mmol/l)	-0.474	0.000*	-0.235	0.076	-0.447	0.000*
TAG (mmol/l)	-0.279	0.034*	- 0.104	0.439	-0.387	0.003*
HDL (mmol/l)	-0.308	0.019*	0.286	0.029*	0.303	0.021*
LDL (mmol/l)	-0.418	0.001*	0.070	0.603	-0.293	0.026*
TChl:HDL	-0.010	0.938	0.297	0.024*	0.096	0.474
LDL:HDL	0.001	0.994	0.287	0.029*	0.132	0.324

178 * Correlation is significant at the 0.05 level (2-tailed)

179 **Table 5: Correlation of plasma levels of non-enzymatic biomarkers of oxidative stress**
180 **with atherogenic indices and other parameters in diabetic subjects**
181

	MDA		Uric Acid		Albumin	
	r-value	p-value	r-value	p-value	r-value	p-value
BMI (Kg/m^2)	0.230	0.083	0.025	0.852	-0.155	0.244
Pulse (b/m)	0.121	0.366	0.184	0.166	-0.307	0.019*
SBP (mmHg)	0.101	0.450	0.312	0.017*	-0.121	0.366
DBP (mmHg)	0.231	0.081	0.291	0.027*	0.096	0.472
FBS (mmol/l)	0.382	0.003*	0.251	0.057	-0.321	0.014
TChl (mmol/l)	0.512	0.000*	-0.031	0.818	-0.036	0.790
TAG (mmol/l)	-0.336	0.010*	- 0.052	0.697	-0.192	0.149
HDL (mmol/l)	0.168	0.206	-0.073	0.587	-0.113	0.398
LDL (mmol/l)	0.460	0.000*	- 0.048	0.718	0.010	0.938
TChl:HDL	0.147	0.272	-0.057	0.674	0.034	0.798

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LDL:HDL	0.113	0.400	- 0.072	0.591	0.068	0.613

182 * Correlation is significant at the 0.05 level (2-tailed)

183

184 ## 3.2 Discussion

185 Diabetes mellitus is associated with hyperglycemia which induces oxidative stress that is responsible for
186 the various complications associated with the disease [18], which affects the heart, the nerves and the
187 retina resulting into heart disorders [19]. The characteristics of diabetic mellitus such as hyperglycemia,
188 dyslipidemia, inflammation, and oxidative stress affect the vascular wall and thus accelerate
189 atherosclerosis and its clinical complications [10].

190 Oxidative stress reflects an imbalance between the systemic manifestation of reactive oxygen species
191 and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting
192 damage. Oxidative stress depicts the existence of products called free radicals and reactive oxygen
193 species (ROS) which are formed under normal physiological conditions but become deleterious when
194 they are unable to be quenched by the antioxidant systems [31]. There are convincing experimental and
195 clinical evidences that the generation of reactive oxygen species is increased in both types of diabetes
196 and that the onset of diabetes is closely associated with oxidative stress [32]. Free radicals are formed
197 disproportionately in diabetes by glucose autoxidation, polyol pathway and non-enzymatic glycation of
198 proteins [33]. Abnormally high levels of free radicals and simultaneous decline of antioxidant defense
199 systems can lead to the damage of cellular organelles and enzymes, increase lipid peroxidation and
200 development of complications of diabetes mellitus [34].

201 From the results obtained in this study, it is evident that the diabetic patients had much higher glucose
202 and lipids levels (TChol and TAG) when compared with non-diabetic subjects. Increased of theses indices
203 in this work is consistent with Whiting et al. [35] which reported that chronic hyperglycemia could
204 influence the generation of free radicals, which might eventually lead to increase lipid peroxidation and
205 depletion of antioxidants. Significant lipid peroxidation, higher levels of lipids and lipid risk factors (such as
206 increase in BMI, SBP & DBP) in diabetic subjects in this study are indicators for atherogenic changes

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207 [36]. The products of lipid peroxidation are harmful to most cells in the body and are associated with a
208 variety of diseases, such as atherosclerosis and brain damage [37].

209 The major finding of this study was that antioxidant levels, both enzymatic and non-enzymatic, were
210 either significantly reduced or increased in diabetic subjects. Significantly decrease in albumin levels and
211 elevated levels of uric acid in the diabetic subjects when compared with the corresponding control groups
212 are reflective of the acute phase response. Acute-phase reactants are plasma proteins that alter in
213 concentration sequel to an inflammatory stimulus [38]. Thus, decrease in plasma levels of albumin may
214 be used as a marker of negative acute phase proteins in type 2 diabetic subjects.

215 Significantly increased mean levels of plasma Uric acid in diabetic cases when compared to controls is
216 associated with higher risk of type 2 diabetes, independent of obesity, dyslipidemia and high blood
217 pressure as reported by Dhengan et al. [39]. In humans, uric acid is the main plasma antioxidant followed
218 by vitamin C and thus, it stabilizes vitamin C in plasma and protects it from oxidation [40, 41]. Besides
219 that hyperuricaemia was presumed to be consequence of insulin resistant [39], Uric acid in the blood had
220 also been documented to scavenge superoxide radicals, hydroxyl radicals, singlet oxygen and could
221 chelate transition metals [42]. Thus increase in plasma levels of Uric acid in cases compared to controls
222 might be a compensatory mechanism to mump up free radicals generated in diabetic condition.

223 This study shows a significant increase in plasma MDA levels in type 2 diabetics when compared to
224 controls indicating increase lipid peroxidation. Malondialdehyde (MDA) is a product of lipid peroxidation
225 and provides a means of assessing the extent of lipid peroxidation. Our data show plasma levels of MDA
226 had significant positive correlation with FBS and TChol. This finding is in agreement with previous report
227 by Suchitra et al. [36] who also reported significant positive correlation of MDA with FBS and TChol in
228 diabetic subjects. This correlation analysis also suggests that hyperglycemia per se is greatly involved in
229 oxidative stress resulting in increased lipid peroxidation.

230 The significant reduction in activity of serum antioxidant enzymes such as SOD, CAT and GPx was
231 recorded in this work among diabetic subjects when compared to controls. This observation is consistent
232 with most invivo and invitro studies which demonstrated that the levels of antioxidant enzymes are altered

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233 in chronic conditions [43]. Catalase catalyzes the decomposition of hydrogen peroxide to water and
234 oxygen. It is a very important enzyme in protecting the cell from oxidative damage by reactive oxygen
235 species (ROS) [44]. Superoxide dismutases are important antioxidant defense systems in nearly all cells
236 exposed to oxygen, they are proteins co-factored with copper and zinc, or manganese, iron, or nickel,
237 while GPx is a selenium dependent enzyme with peroxidase activity whose main biological role is to
238 protect the organism from oxidative damage. The biochemical function of glutathione peroxidase is to
239 reduce lipid hydroperoxides to their corresponding alcohols and to reduce free hydrogen peroxide to
240 water [45]. Oxidative stress results when there is increased production of free radicals or decreased
241 activity of counter-actors, antioxidants or both in a combination [36]. These observations provide evidence
242 why there is increased in the oxidative stress among type 2 diabetes.

243 **4.0 Conclusion and recommendations**

244 The findings of this study show significant differences in dyslipidemia, lipid peroxidation and increasing of
245 oxidative stress markers from naïve type 2 diabetic subjects through controls. Thus, early diagnosis and
246 management of this condition is necessary in order to incorporate antioxidant supplement as a supportive
247 therapy for adequate glycaemic control. This would go far in preventing development of oxidative stress-
248 associated diabetic complications.

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