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Assessment of serum levels of 8-hydroxy-2' deoxyguanosine and f2-isoprostanes in newly diagnosed adult hypertensive with clinical depression in NAUTH, Nnewi, Nigeria

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Abstract

Despite the high prevalence of depression and hypertension, the relationship between the two diseases has received little attention. The potential roles of some biomarkes of oxidative stress in disease progression and management is very crucial. Aim: The present study therefore, evaluated the serum levels of 8-hydroxy-2' deoxyguanosine (8-OHdG) and F-2 isoprostanes in newly diagnosed hypertensive individuals with and without depression at Nnamdi Azikiwe University Teaching Hospital, Nnewi. Method: This was a cross sectional study carried out on randomly selected 121 consented adult male and female participants within the ages of 18-65 years which comprises 30 newly diagnosed hypertensive individuals without depression (Hypertensive), 31 hypertensive individuals with depression selected from the department of internal medicine. 30 non hypertensive with depression (Depressive) and 30 apparently healthy non-hypertensive individuals without depression which served as control selected among the hospital staff. Their bio-data was obtained from their hospital records. 3 ml of venous blood were collected from each of the participants, dispensed into a plain container, centrifuged and serum separated into another container and stored at -20 ^{0}C for the assessment of serum 8-OHdG using Enzyme Linked Immunosorbent Assay (ELISA) Method. Result: The result showed that Hypertensive individuals with and without clinical depression (107.08±22.05, 129.16±82.49) had significantly higher serum level of 8-OHdG when compared with control group (53.95±28.25) ($P<0.05$ respectively). Hypertensive individuals (129.16±82.49) also had significantly higher 8-OHdG level when compared with non-hypertensive with depression (63.31±37.30) ($P<0.05$). Hypertensive individuals with depression (9.94±7.14) and depressive individuals (8.99±5.84) also had significantly higher F2-Isoprostanes level when compared with control (5.15±1.47) ($P<0.05$ respectively). There was a moderately strong positive correlation between 8-OHdG level and body mass index in both hypertensive and depressive individuals ($r=0.682$, $P<0.05$). Conclusion: The study observed higher 8-OHdG and F2-Isoprostanes in individuals with hypertension with and without clinical depression. In addition, there is evidence that oxidative stress is related to inflammation and endothelial activation in individuals with both conditions leading to disease severity.

Keywords: Hypertension; Clinical depression; 8-OHdG; F2-Isoprostanes; Oxidative stress

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1. Introduction

Hypertension, commonly known as high blood pressure, is a very important global public health challenge with far-reaching implications [1]. It is a chronic medical condition characterized by elevated blood pressure levels in the arteries. Hypertension affects people of all ages and is a major risk factor for cardiovascular diseases (CVDs), including coronary heart disease and stroke [2]. The prevalence of hypertension has been steadily increasing over the years, making it a leading cause of morbidity and mortality worldwide Nigeria inclusive [3]. Several factors, contribute to the development and exacerbation of hypertension. Lifestyle factors, such as unhealthy dietary patterns, physical inactivity, smoking, and excessive alcohol consumption, have been linked to hypertension [4]. Genetic and physiological factors also play a role, with heritability estimates suggesting a genetic component to blood pressure regulation [5].

Hypertension is associated with a wide range of health complications, including heart attacks, strokes, kidney disease, and cognitive decline [6]. Moreover, the economic burden of hypertension is substantial, encompassing healthcare costs, medication expenses, and lost productivity more especially in developing countries including Nigeria [3, 7].

Depression on the other hand, is a common mental disorder. Globally, it is estimated that 5% of adults suffer from the disorder. It is characterized by persistent sadness and a lack of interest or pleasure in previously rewarding or enjoyable activities. It can also disturb sleep and appetite. Tiredness and poor concentration are common. Depression is a leading cause of disability around the world and contributes greatly to the global burden of disease. The effects of depression can be long-lasting or recurrent and can dramatically affect a person's ability to function and live a rewarding life. The causes of depression include complex interactions between social, psychological and biological factors. Life events such as childhood adversity, loss and unemployment contribute to and may catalyze the development of depression. Psychological and pharmacological treatments exist for depression. However, in low- and middle-income countries, treatment and support services for depression are often absent, neglected or under developed. It is estimated that more than 75% of people suffering from mental disorders in Nigeria do not receive treatment [8].

The inter-relationship between depression and hypertension have been severally documented. Studies have suggested that individuals with depression may be at a higher risk of developing hypertension and vice versa [9]. Depression can activate physiological stress responses in the body, leading to increased levels of stress hormones, inflammation, and changes in autonomic nervous system activity. These factors may contribute to the development of hypertension [10]. Some medications used to treat depression, such as selective serotonin reuptake inhibitors (SSRIs), may have an impact on blood pressure. Study has shown that depression was associated with decreased blood pressure, though the use of antidepressants was linked to an increased risk of hypertension [11]. The coexistence of these conditions can complicate treatment strategies and worsen prognoses.

Oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) and antioxidants, is implicated in the pathogenesis of both hypertension and depression. Biomarkers such as 8-OHdG and F2-isoprostanes are utilized to measure oxidative damage to DNA and lipids, respectively. 8-OHdG is a biomarker of oxidative DNA damage. Elevated levels of 8-OHdG in urine, blood, or tissues may suggest increased oxidative stress and damage to DNA [12].

F2-Isoprostanes have been identified as important markers related to angiogenesis and oxidative stress, respectively [13]. However, their levels and potential interaction in hypertensive individuals with and without depression remain poorly understood. Understanding the levels of these biomarkers in patients with hypertension and depression may provide insights into the interplay between these conditions and inform therapeutic approaches.

2. Materials and methods

2.1. Study Site

This study was conducted on hypertensive individuals with and without clinical depressive disorders at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria.

2.2. Study Design

A cross sectional study was conducted to evaluate the serum level of 8-OHdG and F2-Isoprostanes in hypertensive individuals with and without clinical depressive disorders in the department of internal medicine at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria. Apparently healthy individuals who were neither hypertensive nor having clinical depression were selected from the hospital staff and served as control. The participants were age matched individuals within the ages of 18-65 years. Consent was sought and obtained from all

the participants using well-structured questionnaire while, their bio data and other medical history were obtained from their hospital records. A total number of 121 participants were selected for this study which comprises 30 hypertensive individuals without depression, 31 hypertensive individuals with depression, making a total of 61 hypertensive individuals and 30 apparently healthy individuals who had neither hypertension nor depression and served as control while the remaining 30 individuals were non hypertensive with depression.

2.3. Inclusion and exclusion criteria

Newly diagnosed adult hypertensive individuals with and without clinical depressive disorders were randomly selected for the study. Apparently healthy participants without clinical depression or hypertension were also selected as control. They were age matched individuals within the ages of 18-65 years. Individuals with malaria infection, Diabetes mellitus and other chronic immune diseases were excluded from the study. Also individuals not within the required age bracket were excluded. Individuals who have been on anti-hypertensive and or on antidepressant drugs were also excluded from the study.

2.4. Ethical approval

The ethical approval for the research was obtained from the board of ethics committee of Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, Nigeria,

2.5. Sample Collection

Three ml (3ml) of venous blood was collected from each of the participants and dispensed into plain containers, allowed to clot, centrifuged at 4000 rpm for 10 minutes and then the serum was extracted into another plain container which was accurately labelled with the subjects accurate details and the samples were transported to the laboratory for analysis.

2.6. Methods

2.6.1. Screening for Clinical Depressive Disorder

Patient Health Questionnaire (PHQ-9) depressive symptom scale containing 09 items was used. It was a Likert scale with the following response options: Patient health questionnaire (PHQ-9) depressive symptom scale have 09 items. 0 = not at all, 1 = several days, 2 = more than half the days, and 3 = nearly every day. Classification of depression was measured by verbal responses of participants to PHQ-9 scale and expressed in scores. PHQ-9 was categorized as follows: severe depression: respondent with a score between 20 and 27; moderately severe depression: respondent with a score between 15 and 19; moderate depression: respondent with a score between 10 and 14; mild depression: respondent with a score between 5 and 9; minimal depression: respondent with a score between 1 and 4; and non-depressed respondent with score 0 [14]. The internal consistency of this instrument using Cornbrash's alpha was 0.883.

2.6.2. Screening for Hypertension

The participants were screened using a micro life digital sphygmomanometer and the results obtained were compared to the reference which states that if systolic and diastolic blood pressure is consistently above 140 mmHg and 90 mmHg respectively in more than two visits, the patient will be a diagnosed hypertensive [15].

2.6.3. Determination of 8-OHdG

The serum level of 8-hydroxy-2-deoxyguanosine was determined using the Competitive ELISA method as described by [16].

Principle

8-OHdG ELISA assay uses a competitive format wherein a murine monoclonal antibody to 8-OHdG (Primary Antibody) and sample or standard are added to a microtiter plate which has been pre-coated with 8-OHdG. Sample or calibrator 8-OHdG competes with plate-bound 8-OHdG for binding with the antibody. Accordingly, higher concentrations of sample or calibrator lead to reduced binding of the antibody to the 8-OHdG coated on the plate. A subsequent wash step removes any free 8-OHdG/antibody adduct leaving a stationary plate bound 8-OHdG complexed to antibody for later detection. Anti-murine antibody conjugated to horseradish peroxidase (HRP-Conjugate) is then added to the plate. HRP-conjugate binds to remaining murine anti-8-OHdG and unbound HRP-conjugate is removed in another wash step. Addition of 3,3',5,5 tetramethylbenzidine (TMB Substrate) results in blue colour development proportional to the amount of anti 8-OHdG antibody bound to the plate and inversely proportional to the concentration 8-OHdG in original

samples or calibrators applied to the plate. The reaction is terminated by addition of phosphoric acid (Stop Solution) producing yellow colour with measurable absorbance at 450 nm. (Northwest life science specialties).

2.6.4. Determination of F-2 isoprostanes

The ELISA method was used for the determination of F-2 isoprostanes [17].

Principle

The kit assay Human F2-isoPs level in the sample, use purified Human F2-isoPs antibody to coat microtiter plate wells, make solid-phase antibody, then add F2-isoPs to wells. Combined F2-isoPs antibody which with HRP labeled, become antibody - antigen – enzyme – antibody complex, after washing completely, Add TMB substrate solution, TMB substrate becomes blue color at HRP enzyme- catalyzed, reaction is terminated by the addition of a sulphuric acid solution and the colour change is measured spectrophotometrically at a wavelength of 450nm. The concentration of Human F2-isoPs in the samples is then determined by comparing the O.D of the samples to the standard curve.

2.7. Statistical Analysis

Data generated from the study was analyzed using SPSS version 25. Qualitative/categorical variables was analyzed using descriptive statistics and values were presented as frequency and percentages, Quantitative variables was presented as mean ± standard deviation, comparative analysis were carried out using one-way ANOVA, post hoc LSD was used to carry out multiple comparison within the groups, test for relationship was carried out using Pearson's correlation and values was considered significant at $p<0.05$.

3. Results

3.1. Values Age (year) SBP (mmHg), DBP (mmHg) and BMI (Kg/m²) in Hypertensive individuals with and without Depression, Non-hypertensive Individuals with Depression and Control Group

The result showed that there was no significant difference in the mean age value of the study groups ($p\geq0.05$). Hypertensive individuals (142.86±18.75) and hypertensive individuals with depression (131.11±10.54) had a significantly higher systolic blood pressure when compared with control individuals (112.60±9.80) ($p<0.05$). Similarly, hypertensive individuals (142.86±18.75) had a significantly higher systolic blood pressure compared with non-hypertensive individuals with depression (115.00±7.07) ($p<0.05$). However, hypertensive individuals with depression (131.11±10.54) had a significantly lower mean systolic blood pressure when compared with hypertensive individuals (142.86±18.75) ($p<0.05$). It was also seen that hypertensive individuals (90.95±9.44) and hypertensive individuals with depression (88.89±12.69) had significantly higher diastolic blood pressure when compared with control individuals (75.90±7.99) ($p<0.05$). Additionally, hypertensive individuals (90.95±9.44) had significantly higher diastolic blood pressure compared to their counterparts with depression (76.80±6.68) ($p<0.05$). Hypertensive individuals (30.88±7.02) and hypertensive individuals with depression (30.86±6.46) had significantly higher body mass index when compared with control individuals (23.57±5.51) ($p<0.05$) (table 1).

Table 1 Values Age, SBP, DBP and BMI in Hypertensive individuals with Depression, Hypertensive, Depressive and Control Group

Group	Age (years)	SBP (mmHg)	DBP (mmHg)	BMI (Kg/m²)
A (n=30)	51.21±9.82	131.11±10.54	88.89±12.69	30.86±6.46
B (n=31)	47.33±7.32	142.86±18.75	90.95±9.44	30.88±7.02
C (n=30)	50.48±9.38	115.00±7.07	76.80±6.68	26.74±6.12
D (n=30)	47.00±10.82	112.60±9.80	75.90±7.99	23.57±5.51
F-value	1.099	20.138	12.071	5.461
p-value	0.354	0.000*	0.000*	0.002*
A VS B	0.147	0.033*	0.573	0.994
A VS C	0.841	0.012	0.006	0.161

A VS D	0.200	0.001*	0.001*	0.006*
B VS C	0.219	0.000*	0.000*	0.093
B VS D	0.884	0.000*	0.000*	0.000*
C VS D	0.270	0.648	0.800	0.200

A- Hypertensive individuals with depression, B- Hypertensive, C- depressive, D- Control; * Significant mean difference at P<0.05.

3.2. Serum level 8-OHdG (ng/L) and F2-Isoprostanes in Hypertensive individuals with and without Depression, Depressive and Control Group

The result showed that hypertensive individuals (129.16±82.49) and hypertensive with depression (107.08±37.30) had significantly higher serum 8-OHdG level when compared with control group (53.95±28.25) (P<0.05). Hypertensive individuals with depression (107.08±37.30) had a significantly higher 8-OHdG level compared with depressive individuals (63.31±22.05). Hypertensive individuals with depression (9.94±7.14) and depressive individuals (8.99±5.84) also had significantly higher F2-Isoprostanes level when compared with control (5.15±1.47) (P<0.05 respectively) (table 1).

Table 2 Serum levels of 8-OHdG and F2-Isoprostanes in Hypertensive Individuals with depression, Hypertensive, Depressive and Control Group

Group	**8-OHdG (ng/L)**	**F2-Isoprostanes (ng/L)**
Hypertensive with depression (A) (n=30)	107.08±37.30	9.94±7.14
Hypertensive (B) (n=31)	129.16±82.49	6.14±3.50
Depressive (C) (n=30)	63.31±22.05	8.99±5.84
Control (D) (n=30)	53.95±28.25	5.15±1.47
F-value	7.564	4.397
P-value	0.000*	0.195
A VS B	0.315	0.477
A VS C	0.027	0.846
A VS D	0.019*	0.014*
B VS C	0.003*	0.245
B VS D	0.000*	0.756
C VS D	0.660	0.027*

* Significant mean difference at P<0.05.

3.3. Serum Level 8-OHdG and F2-Isoprostanes based on Gender in Hypertensive Individuals with Depression, hypertensive, Depressive and Control Group

The result showed that serum level of 8-0HdG was significantly higher in male hypertensive (152.35±72.60) and depressive (82.55±28.67) individuals when compared with their female counterparts (98.25±25.68,) (p< 0.05). Similar observation was made in non-male hypertensive with depression (82.55±28.67) when compared with their female counterparts (98.25±25.68, 44.07±25.25) (p < 0.05 respectively). Conversely, the serum level of 8-OHdG was significantly higher in female hypertensive with depression (105.65±37.19) when compared with female depressive individuals (44.07±25.25) (p<0.05). The serum 8-OHdG level was significantly lower in male hypertensive with depression (112.09±50.00) when compared with hypertensive individuals (152.35±72.60) (p<0.05). Consistently, there was significantly higher level of serum 8-OHdG level in hypertensive with (112.09±50.00) and without (152.35±72.60) depression when compared with depressive (82.55±28.67) and control individuals (47.98±33.53) (p<0.05 respectively). Similarly, serum 8-OHdG level was significantly higher in female hypertensive with depression (105.65±37.19) and hypertensive (98.25±25.68) when compared with depressive (44.07±25.25) and control (61.24±19.5) individuals (p<0.05 respectively). However, no significant differences was found in F2-isoprostane levels among the study gender groups. (P > 0.05) (table 3).

Table 3 Serum level of 8-OHdG and F2-Isoprostanes based on Gender in Hypertensive individuals with depression, hypertensive, depressive and Control Group

Group		Female	Male	t-value	P-value
Hypertensive with depression (A)(f=16, m=14)	8-OHdG F2-Isopros	105.65±37.191 0.64±5.15	112.09±50.00 9.54±4.77	-0.344 0.084	0.482 0.775
Hypertensive (B)(f=15, m=16)	8-OHdG F2-Isopros	98.25±25.68 7.76±1.49	152.35±72.60 7.91±3.18	5.537 0.565	0.001* 0.691
Depressive (C)(f=16, m=14)	8-OHdG F2-Isopros	44.07±25.25 8.62±4.45	82.55±28.67 8.87±3.17	3.833 0.469	0.039* 0.847
Control D (f=14, m=16)	8-OHdG F2-Isopros	61.24±19.54 5.80±1.89	47.98±33.53 6.18±0.98	-1.046 0.392	0.306 0.704
F- value		4.629	7.991	-	-
P-value		0.000	0.000	-	-
A VS B		0.874	0.038*	-	-
A VS C		0.006*	0.162	-	-
A VS D		0.017*	0.003*	-	-
B VS C		0.002*	0.001*	-	-
B VS D		0.035*	0.001*	-	-
C VS D		0.301	0.145	-	-

* Significant mean difference at P<0.05.

3.4. Correlation of serum level of 8-OHdG and F2-Isoprostanes with SBP, DBP and BMI in Hypertensive with and without Depression.

BMI There was a strong positive correlation between the 8-OHdG level and BMI in both hypertensive and depressive individuals (r=0.682, P<0.05).

There was no significant correlation between serum 8-OHDG, DBP and BMI in hypertensive individuals with and without depression (P≥0.05)

Table 4 Correlation of 8-OHdG and F2-Isoprostanes with DBP, SBP and BMI in Hypertensive individuals with and without Depression.

Group	A (n=30)		B (n=31)		C (n=30)		D (n=30)	
Parameters	R	P	R	P	R	P	R	P
8-OHdG VS Age	0.474	0.197	-0.208	0.366	0.404	0.247	0.394	0.086
8-OHdG VS SBP	0.165	0.670	-0.168	0.467	0.057	0.875	0.048	0.841
8-OHdG VS DBP	-0.550	0.125	-0.141	0.543	-0.538	0.109	-0.147	0.536
8-OHdG VS BMI	0.682*	0.043	0.096	0.678	-0.042	0.909	0.259	0.270
F2-Isoprostanes VS Age	0.239	0.479	-0.184	0.451	0.054	0.881	-0.202	0.393
F2-Isoprostanes VS SBP	-0.103	0.764	0.440	0.059	0.101	0.781	0.447*	0.048
F2-Isoprostanes VS DBP	0.146	0.668	0.297	0.217	-0.426	0.220	-0.524*	0.018
F2-Isoprostanes VS BMI	0.174	0.610	-0.020	0.936	-0.141	0.696	-0.160	0.502

A- Hypertensive individuals with depression, B- Hypertensive, C- depressive, D- Control. Pearson correlation, * Significant correlation at P<0.05.

4. Discussion

Hypertension and depression most common pathologies related to poor prognosis when both are associated. A similar mechanism of both conditions involves oxidative stress expressed by such biomarkers as 8-hydroxy-2'-deoxyguanosine (8-OHdG) and F2-isoprostanes, with the first one reflecting oxidative DNA damage and the second standing for lipid peroxidation injury. High levels of these biomarkers point to increased oxidative stress associated with the development of disease.

The present study observed that hypertensive individuals and hypertensive with clinical depression had significantly higher serum 8-OHdG level when compared with control group Elevated serum 8-OHdG level has been observed earlier in individuals with hypertension compared to normal subjects [18]. The oxidative DNA damage has also been associated with endothelial dysfunction, reflected in impaired relaxation and dilation of the blood vessels, thus promoting hypertension. Indeed, excessive oxidative stress outpaces the body's endogenous antioxidant defenses and can stimulate chronic inflammation, vascular remodeling, and hypertension as part of its sequelae [12, 18, 19]. The body has natural antioxidant defenses to counteract oxidative stress. When these defenses are overwhelmed, as can occur in hypertension, oxidative damage may accumulate. Lifestyle factors such as diet, exercise, and exposure to environmental toxins can influence the balance between oxidative stress and antioxidant defenses [20].

Our study observed significantly higher F2-Isoprostanes level in hypertensive individuals with depression and depressive individuals when compared with control participants. Oxidative stress is also involved in the pathophysiology of depression. High levels of F2-isoprostane in depressed persons indicate that lipid peroxidation impairs the structure and signaling of neurons, impairs neuroplasticity, and disturbs neurotransmitter balance, for instance, serotonin, dopamine, and glutamate. Loss of neuroplasticity was related to the severity of depressive symptoms and was enhanced by neuroinflammation [21, 22].

Consequently, both hypertensive and depressive individuals have shown to develop enhanced oxidative stress as compared with controls, represented by two biomarkers, 8-OHdG and F2-isoprostanes. This suggests a common path where oxidative stress is integral in the pathophysiology leading to endothelial dysfunction seen in hypertension and neuroinflammation seen in depression. While the levels of 8-OHdG are associated in a consistent manner with the severity of hypertension and the degree of organ damage, the relation of F2-isoprostanes to hypertension is not well established, in view of the failure of some studies to demonstrate any significant correlation [23, 24]. High levels of F2-isoprostanes, however, indicate lipid peroxidation and renal dysfunction in hypertensive patients [25].

Hypertensive individuals and hypertensive individuals with depression had significantly higher body mass index when compared with control individuals. This is consistent with the previous finding by Luo et al., [26]. The author documented evidence of disease progression and severity when both conditions are present in obese individuals.

5. Conclusion

Understanding the profile of oxidative stress in hypertensive patients with or without depression may provide useful information that is very helpful in therapeutic interventions. Such antioxidant therapy targeting oxidative damage may prevent the progression of disease. These could be supported by pharmacological treatments that address oxidative pathways, including antioxidant-rich diets, regular exercises, and stress management techniques. The measurement of biomarkers 8-OHdG and F2-isoprostanes in newly diagnosed patients opens a window into disease mechanisms that inform personalized strategies for treatment. Future studies shall therefore focus on how these biomarkers can help in the selection of adequate therapies aimed at improving the prognosis of patients with various chronic diseases.

Compliance with ethical standards

Acknowledgment

Authors wish to acknowledge all the participants who voluntarily gave their informed consent for the study.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Reference

[1] Bakris, G., Hill, M., Mancia, G., Steyn, K., Black, H. R., Pickering, T., and Mensah, G. (2008). Achieving blood pressure goals globally: five core actions for health-care professionals. A worldwide call to action. *Journal of Human Hypertension*, *22*(1), 63-70.

[2] Fuchs, F. D., and Whelton, P. K. (2020). High blood pressure and cardiovascular disease. *Hypertension*, *75*(2), 285-292.

[3] Ukibe NR, Alex JC, Osakue NO, Ukibe EG, Ukibe BC, Ukibe EV and Obeagu EI. Linking Malaria and Hypertension: Unveiling the Interconnected Pathophysiological Nexus. IDOSR *Journal of Scientific Research* 9(1) 12-19, 2024. https://doi.org/10.59298/IDOSRJSR/2024/1.1.1219.100 ISSN: 2550-794X IDOSRJSR1.1.1219.100

[4] Ng, R., Sutradhar, R., Yao, Z., Wodchis, W. P., and Rosella, L. C. (2020). Smoking, drinking, diet and physical activity—modifiable lifestyle risk factors and their associations with age to first chronic disease. *International journal of epidemiology*, *49*(1), 113-130.

[5] Padmanabhan, S., Newton-Cheh, C., and Dominiczak, A. F. (2012). Genetic basis of blood pressure and hypertension. *Trends in Genetics*, *28*(8), 397-408.

[6] Meissner, A. (2016). Hypertension and the brain: a risk factor for more than heart disease. *Cerebrovascular diseases*, *42*(3-4), 255-262.

[7] Tarus, A. J. (2022). *Economic Costs of Hypertension-diabetes Mellitus Comorbidity in Primary Public Health Facilities in Kiambu County, Kenya* (Doctoral dissertation, University of Nairobi).

[8] World Health Organization. (2017). *Depression and other common mental disorders: global health estimates* (No. WHO/MSD/MER/2017.2). World Health Organization.

[9] Meng, L., Chen, D., Yang, Y., Zheng, Y., and Hui, R. (2012). Depression increases the risk of hypertension incidence: a meta-analysis of prospective cohort studies. *Journal of hypertension*, *30*(5), 842-851.

[10] Won, E., and Kim, Y. K. (2016). Stress, the autonomic nervous system, and the immune-kynurenine pathway in the aetiology of depression. *Current neuropharmacology*, *14*(7), 665-673.

[11] Bergantin, L. B. (2020). Depression raises the risk of hypertension incidence:discussing the link through the Ca2+/cAMP signalling. *Current Hypertension Reviews*, *16*(1), 73-78.

[12] Valavanidis, A., Vlachogianni, T., and Fiotakis, C. (2009). 8-hydroxy-2′-deoxyguanosine (8-OHdG): a critical biomarker of oxidative stress and carcinogenesis. *Journal of environmental science and health Part C*, *27*(2), 120-139.

[13] Jomova, K., Raptova, R., Alomar, S.Y. *et al.* Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. *Arch Toxicol* **97**, 2499–2574 (2023). https://doi.org/10.1007/s00204-023-03562-9

[14] Beard C, Millner AJ, Forgeard MJ, Fried EI, Hsu KJ, Treadway MT, Leonard CV, Kertz SJ, Björgvinsson T. Network analysis of depression and anxiety symptom relationships in a psychiatric sample. Psychol Med. 2016 Dec;46(16):3359-3369. doi: 10.1017/S0033291716002300. Epub 2016 Sep 14. PMID: 27623748; PMCID: PMC5430082.

[15] Tinawi, M. (2022). New trends in the diagnosis and management of hypertension. *Cureus*, *14*(2).

[16] Van Weemen BK, Schuurs AH. Immunoassay using antigen-enzyme conjugates. FEBS Lett. 1971 Jun 24;15(3):232-236. doi: 10.1016/0014-5793(71)80319-8. PMID: 11945853.

[17] Milne GL, Sanchez SC, Musiek ES, Morrow JD. Quantification of F2-isoprostanes as a biomarker of oxidative stress. Nat Protoc. 2007;2(1):221-6. doi: 10.1038/nprot.2006.375. PMID: 17401357.

[18] Steyers III, C. M., and Miller Jr, F. J. (2014). Endothelial dysfunction in chronic inflammatory diseases. *International journal of molecular sciences*, *15*(7), 11324-11349

[19] Biswas, I., and Khan, G. A. (2020). Endothelial dysfunction in cardiovascular diseases. *Basic Clin Underst Microcirc*, *10*.

[20] Engwa, G. A., Nweke, F. N., and Nkeh-Chungag, B. N. (2022). Free radicals, oxidative stress-related diseases and antioxidant supplementation. *Alternative Therapies in Health & Medicine*, *28*(1).

[21] Alvarez-Mon MA, Ortega MA, García-Montero C, Fraile-Martinez O, Monserrat J, Lahera G, Mora F, Rodriguez-Quiroga A, Fernandez-Rojo S, Quintero J, Alvarez-Mon M. Exploring the Role of Nutraceuticals in Major Depressive Disorder (MDD): Rationale, State of the Art and Future Prospects. Pharmaceuticals (Basel). 2021 Aug 21;14(8):821. doi: 10.3390/ph14080821. PMID: 34451918; PMCID: PMC8399392.

[22] Solleiro-Villavicencio H, Rivas-Arancibia S. Effect of Chronic Oxidative Stress on Neuroinflammatory Response Mediated by CD4+T Cells in Neurodegenerative Diseases. Front Cell Neurosci. 2018 Apr 27;12:114. doi: 10.3389/fncel.2018.00114. PMID: 29755324; PMCID: PMC5934485.

[23] P, Ormezzano O, et al. Lipid peroxidation is not increased in patients with untreated mild-to-moderate hypertension. Hypertension 2003;41(2):286-8.

[24] Ward NC, Hodgson JM, Puddey IB, et al. Oxidative stress in human hypertension: association with antihypertensive treatment, gender, nutrition, and lifestyle. Free Radical Biology & Medicine 2004;36(2):226-32.

[25] Melton, Charles, "Oxidative Status and Hypertension: An Examination of the Prospective Association Between Urinary F2-isoprostanes and Hypertension." Thesis, Georgia State University, 2015. doi: https://doi.org/10.57709/6466444

[26] Luo, Q., Bao, K., Gao, W., Xiang, Y., Li, M., & Zhang, Y. (2023). Joint effects of depressive status and body mass index on the risk of incident hypertension in aging population: Evidence from a nationwide population-based cohort study. *BMC Psychiatry*, *23*, 608. https://doi.org/10.1186/s12888-023-05105-z