AFRICAN JOURNAL OF MEDICINE and medical sciences

VOLUME 43 NUMBER 1 MARCH 2014

ISSN 1116–4077

Afr. J. Med. med. Sci. (2014) 43, 49-57

Antioxidant status and reproductive hormones in women during reproductive, perimenopausal and postmenopausal phase of life

PS Ogunro[1,4], AA Bolarinde[2], OO Owa[2], AA Salawu[1] and AA Oshodi[3]

Department of Chemical Pathology[1], College of Health Sciences, Ladoke Akintola University of Technology, Osogbo. Department of Obstetrics and Gynaecology[2], Federal Medical Centre, Owo, Ondo State, Department of Clinical Pathology[3], College of Medicine, University of Lagos, Idi-Araba, Lagos, and Malaria Research and Clinical Laboratory[4], College of Health Science, Ladoke Akintola University of Technology, Osogbo, Nigeria

Abstract

Background: Reproductive aging resulting in menopause with permanent cessation of ovarian follicular activity. The progressive loss of estrogen and its protective effects, combined with deficient endogenous antioxidant results in oxidative stress.

Objective: To assess the level of oxidative stress and its relationship with reproductive hormones at various developmental phases of women.

Methods: A total of 186 (65 in Reproductive, 58 in Perimenopausal, and 63 in Postmenopausal phase) participants between the ages of 20-60 years were recruited for the study. Follicle-stimulating hormone(FSH), luteinizing hormone(LH), progesterone, estradiol, total antioxidant status(TAS), malondialdehyde (MDA) and reduced glutathione (GSH); activities of glutathione peroxidase (GSH-Px) ,superoxide dismutase (SOD) and catalase (CAT) levels were all determined.

Results: FSH, LH and MDA levels were significantly increased during perimenopausal and postmenopausal phases compared to reproductive phase; however, estradiol, progesterone, TAS and GSH levels were significantly decreased during perimenopausal and postmenopausal phases compared to reproductive phase. The erythrocyte activities of GSH-Px, SOD and CAT were significantly decreased during perimenopausal and postmenopausal phases compared to reproductive phase. It was observed that MDA showed positive correlation with LH and FSH while a negative correlation with estradiol and progesterone was observed; whereas, antioxidants showed negative correlation with LH and FSH while a positive correlation with estradiol and progesterone.

Conclusion: The present study revealed that normal perimenopausal and postmenopausal phase are associated with oxidative stress. Therefore it may be of benefit when both phases are being managed in term of hormonal deficit if antioxidant is an adjunct.

Keywords: *Antioxidant status, reproductive hormones, reproductive, perimenopausal, postmenopausal*

Résumé

Introduction: Le vieillissement de la reproduction résultant de la ménopause avec l'arrêt définitif de l'activité folliculaire ovarienne. La perte progressive de l'œstrogène et de ses effets de protection, combinée avec les résultats d'antioxydants endogènes déficients dans le stress oxydatif. Cette étude avait pour objectif d'évaluer le niveau de stress oxydatif et sa relation avec les hormones de reproduction à différentes phases de développement des femmes.

Méthodes: Un total de 186 (65 en matière de reproduction, 58 en péri ménopause, et 63 dans la phase post-ménopausique) participants âgés de 20-60 ans ont été recrutés pour l'étude. Les taux de l'hormone folliculostimulante (FSH), l'hormone lutéinisante (LH), la progestérone, l'œstradiol, le statut antioxydant total (SAT), le malondialdéhyde (MDA) et le glutathion réduit (GSH); activité de glutathion peroxydase (GSH-Px), superoxyde dismutase (SOD) et catalase (CAT) ont tous été obtenus.

Résultats: Les taux de FSH, LH et MDA ont augmenté considérablement au cours de la péri ménopause et en post ménopausées phases par rapport à la phase de reproduction ; Cependant, estradiol, progestérone, TAS et BA ont sensiblement diminué au cours des phases péri ménopause et en post ménopause par rapport à la phase de reproduction. Les activités érythrocytaires de GSH-Px, SOD et CAT ont été significativement diminué au cours des phases péri ménopause et en post ménopause par rapport à la phase de reproduction. Il a été observé que MDA a montré une corrélation positive avec LH et FSH tandis qu'une corrélation négative avec l'estradiol et de progestérone a été

Correspondence: Dr. P.S. Ogunro, Department of Chemical Pathology, College of Health Science, Ladoke Akintola University, Osogbo, Nigeria. E-mail: ogunrops@yahoo.com

aliquot of supernatant was reacted with 0.67% TBA in a boiling water-bath for 15 min. After cooling, the absorbance was read at 532 nm. Arbitrary values obtained were compared with a series of standard solutions (1,1,3,3 tetramethoxypropane). Measurement of TAS in the plasma was performed using a commercial kit from Randox Laboratories (Randox Laboratories Ltd, Diamond Road, Crumlin, Co. Antrim, Ireland) [24]. The assay was calibrated using 6-hydroxy-2, 5, 8- tetra-methylchroman-2-carboxylic acid (trolox). The results were expressed as mmol/L of trolox equivalent. Measurement of erythrocyte GSH-Px (EC# 1.11.1.9) activity was performed using a commercial kit RANSEL from Randox Laboratories (Randox Laboratories Ltd, Diamond Road, Crumlin, Co. Antrim, Ireland). GSH-Px catalyses the oxidation of GSH to glutathione disulphide(GS-SG) by cumene hydroperoxide, in the presence of glutathione reductase and NADPH. GS-SG is immediately converted to GSH with a concomitant oxidation of NADPH to $NADP^+$ according to the method of Paglia and Valentine[25]. The concentration of GSH-Px activity is assessed from the decrease in absorption at 340nm and at 37°C using Humalyzer 2000 analyzer. A standard curve was prepared by using the standard provided in the kit, and the value for each sample was read from this curve. SOD (EC. 1.15.1.1) activity was estimated by employing xanthine/xanthine oxidase assay commercial kit RANSOD from Randox Laboratories (Randox Laboratories, Crumlin, Antrim, UK) [26]. The results of SOD activity were normalized to the haemoglobin content in the erythrocyte lysate and expressed as U/gHb. The CAT (EC 1.11.1.6) peroxidative activity was measured by the reaction of formaldehyde produced from methanol with purpald to produce a chromophore according to the method of Johansson and Hakan Borg[27]. Quantitation was carried out by measuring the absorbance at 540 nm and comparing the results with those obtained with formaldehyde calibrators. GSH concentration in erythrocytes was determined in the presence of low-molecular-mass free thiol groups, mercuric salt and sulfanilamide, in a highly acidic medium, biazonian salt was produced. The salt so obtained was conjugated with amine salt, producing a coloured complex, the absorbance of which was measured at 535 nm and calculations were made according to the model curve for GSH and expressed in μmoles GSH/g Hb [28].

Statistical analysis

Statistical analysis was performed using SPSS version 11 software. All data were expressed as mean ± SD. One-way ANOVA; paired-sample and independent-sample t- tests were applied where appropriate. Correlations were determined using Pearson's Correlation co-efficient. $P < 0.05$ was considered statistically significant in all comparisons.

Results

Table I: The anthropometric and blood pressure levels of all participants

	Reproductive phase (n=65)	p_1-Value	Women in Perimenopausal phase (n=58)	p_2-Value	Postmenopausal phase (n=63)	p_3-Value
Age(yrs)	25.4±1.8	0.0401[a]	47.5±2.5	0.0095[b]	56.8±1.9	0.0409[a]
Height(cm)	161.01±2.4	0.9561	159.12±2.1	0.8932	160.37±3.5	0.9068
Weight(kg)	61.99±1.3	1.0043	60.87±2.3	0.8942	64.13±4.3	0.8915
BMI	23.92±1.7	0.9071	24.10±2.2	0.8906	24.93±0.2	0.9130
Waist(W) Cirumference(cm)	71.03±2.5	0.9751	70.76±1.9	0.9901	2.05±0.7	0.8947
Hip(H) Circumference(cm)	91.92±2.1	0.9573	90.58±2.7	0.9907	93.13±1.2	0.8432
W/H ratio	0.77±0.02	0.8601	0.78±0.07	1.0231	0.77±0.9	0.8943
Systolic BP (mmHg)	118 .9±2.3	0.7518	121.2±3.5	0.6621	128.6±1.7	0.5017
Diastolic BP (mmHg)	81.3±1.4	0.6981	85.3±2.4	0.3810	88.2±1.2	0.4174

Values are (mean ± SD)

p_1 - Value = Comparism of Perimenopausal with Reproductive Women;

p_2 -Value = Comparism of Postmenopausal with Reproductive Women;

p_3 -Value = Comparism of Postmenopausal with Perimenopausal Women;

Significant level at the ($p < 0.05$)[a] and ($p < 0.01$)[b]

[18]. CAT is a haemeprotein catalyzing the decomposition of H_2O_2 to water and oxygen and GSH-Px is a selenoenzyme which catalyzes the degradation of H_2O_2 and hydroperoxides at the expense of reduced glutathione GSH [18]. In women who have regular menses, estrogen levels peak twice throughout the cycle, once in the late follicular phase and to a lesser degree in the luteal phase [19]. On the contrary, anovulatory women demonstrate a relatively steady-state estradiol level and often have oligo- or amenorrhea [19]. Free oxygen radicals have been implicated as important causative agents of aging [20, 21]. Hence menopausal women are subjected to oxidative stress (OS) through estrogen deficiency and advancing age. Research on the relationship between oxidative stress and reproductive hormone during reproductive phases of women remains unclear and few studies in this area has produced controversial results [22].

To better understand the antioxidant status and its relationship with reproductive hormones we evaluated biomarkers of oxidative stress and reproductive hormones at various reproductive phases of women. We hypothesized that variations in hormonal level during reproductive, perimenopausal and postmenopausal phases of women could affect the antioxidant status and may further contribute to symptoms associated with these reproductive phases.

Materials and methods

Subjects

This study was approved by Ladoke Akintola University of Technology, College of Health Sciences Research Ethical Committee, Osogbo, Osun State, Nigeria. A total of 186 (65 in Reproductive phase, 58 in Perimen pausal phase and 63 in Postmenopausal phase) women between the ages of 20-60 years old were recruited from the community, Primary Health Centres and General hospitals around Osogbo, Osun State, Nigeria. Paticipants who were healthy, sedentary, non-obese (BMI <26) and waist to hip (W/H) circumference ratio of <0.8 were enrolled in the study. The participants that fulfilled inclusion criterias were randomly selected for the study.

Women in Reproductive phase were those who had regular menstrual cycles (28 ± 2 days during the last 6months);women in Perimenopausal phase were those with clinical perimenopausal symptoms, who were evaluated via the questionnaire of the Menopausal Rating Scale; who had ≥10 hot flushes/ wk, had irregular menses or menstrual period cessation, history estimated to last approximately four years covering a year or two before, those who were not excessively exercising [< 10.46 MJ (<2500 kcal) expenditure/wk] and had both ovaries remaining intact. In addition, only those with an elevated follicle stimulating hormone concentration (≥30 IU/L) after blood analysis for fertility profiles were finally include in the study as perimenopausal women. Postmenopausal women are those with 12 months of amenorrhea in the absence of surgical or hormonal induction after the end of menses.

Excluded from the study are women who are not certain of their menstrual status, smokers, regular alcohol consumers, antioxidant supplement users, pregnant or lactating women, women performing excessive physical exercise, women receiving hormone replacement therapy and women with chronic disease. Blood samples for serum level estimation of FSH, LH, progesterone, estradiol and other parameters were taken a day after menstruation for those in reproductive and perimenopausal(if menstruation occur) phase. Blood samples were collected at 0830 hour, after 12 hours overnight fast into plain and K_2 EDTA bottle. All samples collection procedures were conducted with minimum light exposure, and kept cold in dark until processed in the laboratory. Blood samples in plain bottle were allowed to clot, retract and separated by centrifugation at 1000g for 15 min at room temperature and the serum obtained were stored below -20°C until they are analyzed. Plasma was obtained from K_2EDTA bottle sample by centrifugation at 1000g for 15 min at room temperature within one hour of collection. The red blood cells portion were washed three times with equal volumes of normal saline and centrifuged at 2000 g for 15 min. The washed red blood cells were then hemolyzed in distilled water (1:4, v/v) and by freezing and thawing. The hemolysate was centrifuged and the supernatant and plasma were then stored at –20°C until they were analyzed.

Analytical procedure

Serum level of FSH, LH, progesterone and estradiol were measured using commercially available Human ELSA kits for each parameter[22]. Plasma MDA levels was estimated using the method of Draper and Hadley[23] based on the reaction of MDA with thiobarbituric acid (TBA) at 95°C. In the TBA test reaction, MDA and TBA react to form a pink pigment with an absorption maximum at 532 nm. The reaction was performed at pH 2-3 at 95°C for 15 min. The sample was mixed with 2.5 volumes of 10% (w/v) trichloroacetic acid to precipitate the protein. The precipitate was pelleted by centrifigation and an

perimenopausal and postmenopausal phases compared with the reproductive phase; a significant decrease ($p < 0.05$) was obtained for CAT activity during postmenopausal phase compared to perimenopausal phase. The erythrocyte concentration of GSH was significantly decreased ($p < 0.01$) during perimenopausal and postmenopausal phases compared to reproductive phase.

Tables 3 and 4, show the correlation involving marker of oxidative stress, antioxidant status and reproductive hormones during perimenopausal and postmenopausal phases. During perimenopausal phase, MDA was positively correlated with FSH and LH; but negatively correlated with estradiol and progesterone. Contrarily, antioxidants were negatively correlated with FSH and LH; but positively correlated with estradiol and progesterone. Similarly, during postmenopausal phase, MDA was positively correlated with FSH and LH; but negatively correlated with estradiol and progesterone. Contrarily, antioxidants are negatively correlated with FSH and LH; but positively correlated with estradiol and progesterone.

generation of prooxidant molecules, ROS, including hydroxyl radical, superoxide anion, hydrogen peroxide and nitric oxide. The balance between prooxidants and antioxidants maintain cellular homeostasis, whenever there is an imbalance in this equilibrium, a state of oxidative stress is initiated.

In the present study, it has been shown that circulating level of oxidative stress marker, MDA was significantly increased during perimenopausal and postmenopausal phases compared to reproductive phase of women. Our finding is in agreement with a similar study by Arora *et al.*[29] in which they observed that there is enhanced oxidative stress and decreased antioxidant defence in postmenopausal women when compared with pre-menopausal women. The TAS level, estradiol, progesterone, erythrocytes GSH, erythrocytes activities of GSH-Px, SOD and CAT were significantly reduced in the present study when their values for women in perimenopausal and postmenopausal phases were compared to women in reproductive phase. Several studies had earlier reported antioxidant properties of estradiol; some investigators hypothesis that estrogen has antioxidant

Table 3:. Correlations analysis (r) involving antioxidant status, MDA and reproductive hormones during perimenopausal phase

	MDA	TAS	GSH-Px	SOD	CAT	GSH
FSH	0.5209[c]	- 0.3480[a]	- 0.4179[b]	- 0.3401[a]	- 0.3715[a]	- 0.4531[b]
LH	0.5051[c]	- 0.3112[a]	- 0.4007[b]	- 0.3199[a]	- 0.3201[a]	- 0.4039[b]
Oestradiol	- 0.4416[b]	0.3318[a]	0.3798[a]	0.3107[a]	0.3097[a]	0.3272[a]
Progesterone	- 0.3195[a]	0.2183	0.3270[a]	0.2005	0.2298	0.21864

Values are correlation coefficients (r)
Significant level at the a = ($p < 0.05$), b = ($p < 0.01$) and c = ($p < 0.001$)

Table 4: Correlations analysis (r) involving antioxidant status, MDA and reproductive hormones during postmenopausal phase

	MDA	TAS	GSH-Px	SOD	CAT	GSH
FSH	0.5981[c]	- 0.3556[a]	- 0.4393[b]	- 0.3728[a]	- 0.3297[a]	- 0.4703[b]
LH	0.5182[c]	- 0.3031[a]	- 0.4105[b]	- 0.3418[a]	- 0.3110[a]	- 0.3732[a]
Oestradiol	- 0.4997[c]	0.3204[a]	0.4188[b]	0.3210[a]	0.3205[a]	0.3523[a]
Progesterone	- 0.3315[a]	0.3170[a]	0.3191[a]	0.2056	0.2107	0.3189[a]

Values are correlation coefficients (r)
Significant level at the a = ($p < 0.05$), b = ($p < 0.01$) and c = ($p < 0.001$)

Discussion

The female reproductive system is a complex multiorgan system which requires an optimal biological environment. Aerobic metabolism is essential for this process and it's associated with the

capabilities and other claimed otherwise[30-33]. One of the studies revealed that its decline after menopause predisposes women to increased damage caused by free radicals[34]. A study also showed that estrogen prevents the oxidation of low density

Anthropometric measurements and other clinical parameters of the participants are presented in table 1. All the participants were normotensive, BMI < 26 and W/H ratio < 0.8; however, the age range between the women in perimenopausal and postmenopausal phase were significantly increased compared to women in reproductive phase($p < 0.05$).

The biochemical parameters are shown in table 2. Serum levels of FSH and LH are significantly increased ($p < 0.001$) during perimenopausal and postmenopausal phase compared to reproductive phase; likewise, significant increase ($p < 0.001$) for FSH level and ($p < 0.01$) for LH level were obtained when perimenopausal was compared to postmenopausal phase. Serum level of estradiol was significantly decreased ($p < 0.001$) during perimenopausal and postmenopausal phase compared to reproductive phase; likewise, significant decrease ($p < 0.05$) was obtained when perimenopausal was compared to postmenopausal phase; similarly, progesterone level was significantly decreased ($p < 0.01$) during perimenopausal and postmenopausal phase compared to reproductive phase.

Plasma level of MDA was significantly increased ($p < 0.01$) during perimenopausal and postmenopausal phases compared to reproductive phase; similarly, plasma level of MDA was significantly increased ($p < 0.05$) during postmenopausal phase when compared with perimenopausal phase. However, plasma level of TAS was significantly decreased ($p < 0.05$) during the perimenopausal and postmenopausal phases compared to reproductive phase; likewise, plasma level of TAS was significantly decreased ($p < 0.05$) during postmenopausal phase when compared with perimenopausal phase. The erythrocyte GSH-Px activity was significantly decreased ($p < 0.01$) during perimenopausal and postmenopausal phases compared with reproductive phase; similarly,a significant decrease ($p < 0.05$) of erythrocyte GSH-Px activity was obtained during postmenopausal phase compared with perimenopausal phase. Erythrocyte SOD and CAT activities were significantly decreased ($p < 0.05$) during

Table 2: Hormone, MDA and Antioxidant level of all study participants

	Reproductive phase (n=65)	p_1-Value	Women in Perimenopausal phase (n=58)	p_2-Value	Postmenopausal phase (n=63)	p_3-Value
FSH (IU/L)	6.18±2.7	0.0008[c]	74.68±5.2	0.0000[c]	115.89±12.8	0.0000[c]
LH (IU/L)	9.43±2.1	0.0007[c]	37.88±4.5	0.0000[c]	49.07±6.3	0.0025[b]
Oestradiol (pmol/L)	343.07±23.8	0.0000[c]	107.7±10.3	0.0000[c]	74.68±8.4	0.0405[a]
Progesterone (nmol/L)	2.98 ±0.3	0.0047[b]	0.97±0.03	0.0016[b]	0.56±0.02	0.0748
Plasma-MDA (nmol/ml)	2.71±0.41	0.0060[b]	4.07±0.46	0.0043[b]	5.99±0.18	0.0405[a]
Plasma TAS (mmol/L)	1.98±0.18	0.0304[a]	1 30±0.08	0.0211[a]	1.21±0.09	0.0439[a]
Eryth-GSHPx (U/g Hb)	38.07±4.25	0.0097[b]	22.46±3.80	0.0048[b]	19.85±2.17	0.0415[a]
Eryth-SOD (U/g Hb)	925.26±57.83	0.0420[a]	898.18±51.37	0.0371[a]	864.17±63.19	0.0693
Eryth-CAT (U/g Hb)	1502.84±86.1	0.0435[a]	1295.27±57.9	0.0182[a]	1101.49±44.9	0.0474[a]
Eryth GSH (μmol /g Hb)	7.12±0.8	0.0082[b]	4.07±0.4	0.0045[b]	4.25±0.6	0.0646

Values are (mean ± SD)
p_1-Value = Comparism of Perimenopausal with Reproductive Women;
p_2-Value = Comparism of Postmenopausal with Reproductive Women;
p_3-Value = Comparism of Postmenopausal with Perimenopausal Women;
Significant level at the ($p < 0.05$)[a], ($p < 0.01$)[b] and ($p < 0.001$)[c]

10. Nisar N and Sohoo NA. Severity of Menopausal symptoms and the quality of life at different status of Menopause: a community based survey from rural Sindh, Pakistan. IJCRIMPH. 2010; 2(5): 118-130.
11. Dennerstein L, Dudly EC, Hopper JL, Guthrie JR and Burger HG. A prospective population based study of menopausal symptoms. Obstet Gynecol. 2000; 96: 351-358.
12. Deeks AA and McCabe MP. Well being and menopause: an investigation of purpose in life, self acceptance and social role in pre-menopausal, perimenopausal and postmenopausal women. Qual Life Res.2004;13: 389-398.
13. Lee M, Kim J, Park MS, *et al.* Factors Influencing the Severity of Menopause Symptoms in Korean Post-menopausal Women. J Korean Med Sci. 2010; 25(5): 758-765.
14. Aso T. Demography of the Menopause and Pattern of Climacteric Symptoms in the East Asian region. In: Proceedings of the first consensus meeting on menopause in the East Asian Region, Geneva, 2–30 May 1997. Zeist, Netherlands, Medical Forum International BV, 1998; 24-32.
15. Bokov AF, Ko D and Richardson A. The effect of gonadectomy and estradiol on sensitivity to oxidative stress. Endocr Res. 2009; 34(1-2):43-58.
16. Michos C, Kiortsis DN, Evangelou A and Karkabounas S. Antioxidant Protection during the menstrual cycle: the effects of estradiol on ascorbic dehydroascorbic acid plasma levels and total antioxidant plasma status in eumenorrhoic women during the menstrual cycle. Acta Obstet Gynecol Scand. 2006; 85(8):960-965.
17. Ruiz-Larrea MB, Martin C, Martinez R, *et al.* Antioxidant activities of estrogens against aqueous and lipophilic radicals; differences between phenol and catechol estrogens. Chem Phys Lipids. 2000;105(2):179-188.
18. Gutteridge JMC. Free radicals in disease processes: a compilation of cause and consequence. Free Radic Res Common 1993; 19: 141-158.
19. Speroff L and Fritz MA, editors. Anovulation and the polycystic ovary. Clinical Gynaecologic Endocrinology and Infertility. 7th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2005:465-498.
20. Ogunro PS and Ogungbamigbe TO. Influence of ageing process on body composition of antioxidant and lipid peroxiadtion among healthy individual in south west Nigeria. Nig Postgrad Med J. 2013; 20(1): 39-44.
21. Inal ME, Kanbak G and Sunal E. Antioxidant enzyme activities and malondialdehyde levels related to aging. Clin Chim Acta 2001; 305:75-80.
22. Knobil E. The neuroendocrine control of the menstrual cycle. Recent Prog Horm Res. 1980; 36:53-88.
23. Draper H and Hadley M. Malondialdehyde determination as index of lipid peroxidation. Methods Enzymol. 1990; 186: 421-431.
24. McLemore JL, Beeley P, Thorton K, *et al.* Rapid automated determination of lipid hydroperoxide concentrations and total antioxidant status of serum samples from patients infected with HIV. Am J Clin Pathol. 1998; 109: 268-273.
25. Paglia DE and Valentine UN. Studies on quantitative and qualitative characterization of erythrocyte glutathione peroxidase. J Lab Clin Med. 1967; 70: 158-169.
26. Woollians JA, Wiener G, Anderson PH and McMurray CH. Variation in the activities of glutathione peroxidase and superoxide dismutase and in the concentration of copper in the blood in various breed crosses of sheep. Res Vet Sci. 1983; 34: 253-256.
27. Johansson LH and Hakan Borg LA. A spectrophotometric method for determination of catalase activity in small tissue samples. Anal Biochem.1988; 174: 331-336.
28. Seville B. A scheme for the colorimetric determination of microgram amounts of thiols. Analyst. 1958; 33: 670-672.
29. Arora KS, Gupta N, Singh RA, *et al.* Role of free radicals in menopausal distress. J Clin Diag Res. 2009; 3:1900-1902.
30. Borrás C, Gambini J, López-Grueso R, *et al.* Direct antioxidant and protective effect of estradiol on isolated mitochondria. Biochim Biophys Acta. 2010;1802: 205-211.
31. Sipe HJ, Jordan SJ, Hanna PM and Mason RP. The metabolism of 17 beta-estradiol by lactoperoxidase: a possible source of oxidative stress in breast cancer. Carcinogenesis.1994; 15(11):2637-2640.
32. Okoh V, Deoraj A and Roy D. Estrogen-induced reactive oxygen species-mediated signalings contribute to breast cancer. Biochim Biophys Acta. 2011; 1815:115-133.
33. Fussell CK, Udasin RG, Smith PJS, *et al.* Catechol metabolites of endogenous estrogens induce redox cycling and generate reactive

lipoproteins and stimulates the activities of the antioxidant enzymes[35]. Recently, in vitro studies have demonstrated decreased induction of peroxide production by estradiol in isolated mitochondria; higher activity and expression of genes encoding Mn-SOD and GSH-Px in mitochondria from females mitochondria compared with those of males [30, 36]. Our finding in the present study is in conformity with the above findings in area of reproductive hormone and oxidative stress. However, other studies have demonstrated a pro-oxidant activity of estrogen in which they found that in the mammary environment, the metabolism of 17 β- estradiol by lactoperoxidase can produce reactive phenoxyl radical intermediates[32, 33]. These intermediates give rise to superoxide radicals and their dismutation result in formation and intracellular accumulation of hydrogen peroxide, supporting a role for estrogen-related oxidative stress in the development of breast cancer[31]. In addition, endogenous or synthetic estrogens can be converted to catechol metabolites through aromatic hydroxylation, which give rise to reactive estrogen semi-quinones and quinines[32]. Catechol metabolites of endogenous estrogens have been previously shown to be involved in the redox cycle in breast epithelial cells through generation of reactive oxygen species such as hydrogen peroxide and hydroxyl radicals[33]. However, in our study a strong positive correlation was obtained between MDA and FSH; MDA and LH with a negative correlation between MDA and estradiol; MDA and progesterone among women in perimenopausal and postmenopausal phases. Also in the present study the erythrocyte antioxidant enzyme activities of GSH-Px, SOD and CAT were negatively correlated with FSH and LH; whereas, they were positively correlated with estradiol and progesterone. Studies on the relationship between oxidative stress and reproductive hormone during reproductive phases of women remain unclear and the few studies in this area have produced controversial results. In the present study, we took care to remove confounding factors related to lifestyle of all participants (e.g. obesity, antioxidant use, smoking, regular alcohol consumption, excessive physical exercise, pregnancy, lactation, treatment with hormone replacement therapy, and chronic disease) except for age differences which also have effect on antioxidant status[20]. Our data indicate the novel finding that perimenopausal and postmenopausal women are more susceptible than reproductive women to oxidative stress; also postmenopausal women are more susceptible than perimenopausal women to oxidative stress.

Conclusion

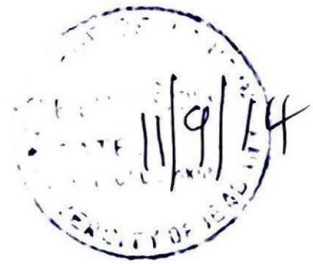
We found that women in perimenopausal and postmenopausal phase of life are under increased oxidative stress. Studies on the relationship between oxidative stress and reproductive hormones on different reproductive phases of women remain unclear and have produced controversial results. In spite of that, this study provides new data in the area of perimenopausal and postmenopausal phases of women in relation to reproductive hormones and oxidative stress. We recommend therefore that when both phases are being managed in term of hormonal deficit, antioxidant supplementation should also be considered as an adjunct for the well being of the individual.

References

1. Valko M, Rhodes CJ, Moncol J, *et al.* Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chem Biol Interact. 2006; 160:1-40.
2. Ridnour LA, Isenberg JS, Espey MG, *et al.* Nitric oxide regulates angiogenesis through a functional switch involving thrombospondin-1. Proc Natl Acad Sci U.S.A. 2005; 102: 13147-13152.
3. de Bruin JP, Dorland M, Spek ER, *et al.* Ultrastructure of the resting ovarian follicle pool in healthy young women. Biol Reprod. 2002; 66:1151-1160.
4. Ray SD, Lam TS, Rotollo JA, *et al.* Oxidative stress is the master operator of drug and chemically-induced programmed and unprogrammed cell death: Implications of natural antioxidants in vivo. Biofactors. 2004; 21: 223-232.
5. Burger HG, Dudley EC, Robertson DM and Dennerstein L. Hormonal Changes in the Menopause Transition. Recent Prog Horm Res. 2002; 57: 257-275.
6. McKinlay SM, Brambilla DJ and Posner JG, The normal menopausal transition. Maturitas. 1992;14:103-115.
7. World Health Organization Geneva, Switzerland. Research on the Menopause in the 1990s. Technical report 1996.Scr 866.
8. Okonofua FE, Lawal A and Bamgbose J. Features of Menopause and Menopausal Age in Nigerian Women. Int J Gynaecol Obstet. 1990; 31: 341-345.
9. Malik HS. Knowledge and attitude towards menopause and Hormone Replacement Therapy (HRT) among postmenopausal women. JPMA. 2008; 58(4): 164-167.

oxygen species in breast epithelial cells. Carcinogenesis. 2011; (0): 1-9.

34. Schwenke DC. Aging, menopause, and free radicals. Semin Reprod Endocrinol. 1998;16: 281-308.
35. Bednarek-Tupikowska G Antioxidant properties of estrogens. Ginekol Pol 2002;73: 61-67.
36. Borrás C, Sastre J, García-Sala D, *et al.* Mitochondria from females exhibit higher antioxidant gene expression and lower oxidative damage than males. Free Radic Biol Med.2003;34(5): 546-552.



maladaptive behaviours, it is referred to as distress [3]. This state of distress is simply referred to as stress on many occasions. Work related stress develops because a person is unable to cope with the demands being placed on him/her. This can affect health, hinder effectiveness at work and lead to low performance, job dissatisfaction, poor motivation, absenteeism and high turnover [4].

Stress appears to be endemic in the current workplace, as surveys have shown that a large number of employees report feeling stressed at work [5]. The growth of industries, pressure in the urban areas, quantitative growth in population and various problems in day to day life are some of the reasons for an increase in stress [6].

Research shows that 54% of Americans are concerned about the level of stress in their everyday lives [7]. Another survey showed that 75% of adults experienced moderate to high levels of stress in the past month while 42% of adults reported that their stress has increased in the past year. Some twenty nine per cent (29%) of workers in another survey reported that they feel quite a bit or extremely stressed at work [8]. A study in Australia reports that 1 in 3 adults suffers from moderate to extreme stress at work and this is an increase of nearly 40% in just 4 years [9].

Stress can lead to mental and physical illness. Many studies have implicated stress in the etiology of a number of psychiatric [10] and physical ailments like flu, cold, arthritis and coronary heart disease [11]. The psychological response includes mood changes, reduced motivation and low self esteem while behavioural response includes aggression, violence or drug addiction [12].

Stress also causes weight changes, obesity in some and weight loss in others [13]. Stress has also been linked to fever [14] depression, cancer and general ill health. In addition, high levels of stress can result in greater health problems such as heart attacks, hypertension, diabetes, ulcerative colitis, strokes, indigestion and heart burn, depression, chronic fatigue syndrome. Workplace stress can greatly influence the personal and social life of people [15,16].

Research shows that stress is not confined to any specific occupation.However, data for different occupational groups such as shown from longitudinal national statistics indicate that particular occupational groups such as those in the financial services are more at risk of stress than other occupations. The financial services sector is traversing a period of major changes resulting from globalization and market deregulation, which has resulted into increased competition especially through merger and acquisition activity in industrialized and developing countries [17].

During the past decade, the Nigerian banking sector had under gone rapid and striking changes like policy changes, increased competition due to the entrance of more private (corporate) sector banks, downsizing, bank deregulation and introduction of new technologies especially in communication and information processing [18].

The banking job is stressful as the operational framework of the bank requires bank workers to resume early and close very late.The introduction of weekend banking (Saturday banking), while some of them are also required to update themselves academically within a set time, which makes most bank workers to register for degree/diploma weekend programmes are other factors in this regard. This is in most cases borne out of compulsion rather than of interest thus creating a stressful situation through conflicting behavioural tendencies [19].

Most bank workers work under tension and the majority seems to remain on the job in order to avoid the pains of unemployment as against the global concept of job satisfaction. Such conditions cannot but produce dissatisfaction and a stressful situation. In fact, the fear of being sacked in the psyche of an average bank worker has its physiological consequences on such individual as job security is very poor these days in the banking sector [20]. Research shows that there is a high level of stress experienced in the Nigerian banking industry due to performance indicators, post traumatic disorder due to increased bank robberies and the introduction of Saturday banking [21-23]. However little is known about the level of knowledge of stress among the bank workers and their mechanisms used to cope with stress. This study therefore assessed the knowledge, prevalence, associated factors and mechanisms of coping with stress among bankers in Lagos State.

Methods

This was a cross-sectional study carried out in Lagos State, the commercial and financial hub of Nigeria. It is heavily populated with over 10 million inhabitants. Due to its commercial nature, several banks and financial institutions are present with a large customer base. The study was conducted in 2 pre-determined local government areas (LGAs) in Lagos State (out of 20), namely Eti-Osa and Lagos Island. They were chosen because they represent the megacities in Lagos State where all banks are