International Journal of Medical and Health Research
ISSN: 2454-9142, Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 3; Issue 8; August 2017; Page No. 19-24

The relationship between age and increasing body weight on oxidative stress and some antioxidants in adult Nigerian male

[1] Eidangbe O George, [*1, 2] Idonije O Blessing, [3] Idemudia J Osagie, [4] Agbebaku O Solomon, [5] Mokogwu A.T Hughs, [6] Festus O Okojie

[1] Department of Medical Biochemistry, College of Medical Sciences, Ambrose Alli University, Ekpoma, Edo State, Nigeria
[2,4] Department of Chemical Pathology, College of Medical Sciences, Ambrose Alli University, Ekpoma, Edo State, Nigeria
[3] Department of Chemical Pathology, School of Medicine, University of Benin, Benin-City, Nigeria
[5] Department of Chemical Pathology, Faculty of Clinical Medicine, Delta State University, Abraka, Nigeria
[6] Department of Medical Laboratory Science, College of Medical Sciences, Ambrose Alli University, Ekpoma, Edo State, Nigeria

Abstract
Background: It has been shown that oxidative stress is implicated in normal processes of life (aging) and the pathogenesis of a wide range of diseases such as obesity. Hence, this study was designed to assess the relationship between age and body weight on oxidative stress and some antioxidants.
Method: Two hundred (200) adult males, between the ages of 18 and 40 years who gave informed consents were recruited as the study population.Their ages (years), weights (Kg), heights (M), Body Mass Index (BMI) and serum levels of Malondaldehyde (MDA), some selected antioxidant vitamins (A and E) were determined using standard procedures.
Results: Results showed that the age (years) correlate positively with MDA (+0.81) but negatively with vitamin A (-0.62) and vitamin E (-0.77). Similarly, body weight (Kg/m^2) was observed to correlate positively with MDA (+0.89) but negatively with vitamin A (-0.82) and vitamin E (-0.82).
Conclusion: Conclusively therefore, the findings of this study suggest that oxidative stress is induced by increasing age and body weight in male. It is therefore our recommendation that male with increasing age and body weight take additional antioxidant supplements from diets and drugs to combat the oxidative stress build-up by physiological processes such as ageing.

Keywords:aging, body mass index, oxidative stress, antioxidant vitamins

Introduction

Although the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) is part of normal aerobic cellular metabolism[1,2,3,4,5], a situation whereby the production of these cellular levels of products of normal aerobic cellular metabolism (ROS or RNS) overwhelm the cellular antioxidant capacities, oxidative stress is said to take place[6]. By implication, oxidative stress can be seen as the imbalance between the products of normal aerobic cellular metabolism (pro-oxidant such as ROS or RNS) and antioxidant substances. While pro-oxidant substances are highly reactive molecules that constantly attack the human body through biochemical reactions or exposure to environmental factors [7,8], antioxidants are substances that prevent or significantly attenuates the oxidation of an oxidizable substrate [9], such as lipids, proteins, carbohydrates and deoxyribonucleic acid – DNA [10].Both substances (pro-oxidant and antioxidant substances) are generated in a redox setting, in which oxidation implies a gain in electrons, and reduction in a loss. Considering that the production and action of pro-oxidant and antioxidant substances depends on this redox system, several studies used the term 'imbalance of the redox system' to refer to 'oxidative stress' [11, 12].

Aging is dynamic, progressive, irreversible and universal, characterized by the occurrence of morphological, biochemical, functional and psychological changes in the organism [13]. The fundamental manifestation of the aging process is a progressive decline in the functional maintenance of tissue homeostasis and an increasing propensity to degenerative diseases and death [14]. It has attracted significant interest to study the underlying mechanisms of aging, and there is an emerging consensus that aging is a multifactorial process, which is genetically determined and influenced epigenetically by environment [15]. On the other hand, in 1956, it was proposed that the aging is partially associated to the accumulation of oxidative damage in biomolecules such as lipids, proteins, carbohydrates and deoxyribonucleic acid (DNA) [10]. This was due to its potential to cause oxidative deterioration of DNA, protein, and lipid, and ROS was therefore implicated as one of the causative factors of aging[10].

Obesity on the other hand; defined as an unhealthy excess of body fat, indicated by mean body weight and body mass index (BMI) has been reported by several studies to gradually increase with age in adult life and reach peak values at 50–59 year in both men and women [16,17,18,19,20].Although it was reported that mean body weight and BMI tend to decrease after age 60 year but this fact was said to be affected by survival bias as obese persons have higher mortality rates [21]. In other several studies, it was shown that body weight and BMI do not change, or decreases only slightly, in older adults

[22,23,24,25]. The combine association of age and body mass therefore lead to the question 'what could be the association between age and BMI on oxidative stress?

It is therefore the aim of this study to investigate the association between increasing age and weight as shown by body mass index on oxidative stress indicated by the level of MDA and some selected antioxidants.

Materials and Methods

Study design: The study design used for this study was a cross-sectional study design.

Study Area: This study was conducted in Ekpoma, Benin City, Kwale and Asaba, all in the south-south zone of Nigeria.The inhabitants of these communities feed mainly on foods like carbonhydrates and beans with western diets like macaroni and spaggetti.

Subjects: The study population is comprised of 200 adult male between the ages of 18 to 40 years.

Ethical Consideration: The study was part of a community based development service. It was conducted in compliance with the Declaration on the Right of the Patient [26]. Before enrolment into the study, informed consent was obtained from all participants.

Ethical approval for the study was obtained from the Local Government Areas Chairmen. The health ethical committee and research proposal was considered and approved by the postgraduate school board of studies, Ambrose Alli University, before the commencement of this study. The community/ Village Heads of the subjects were duly informed and permission sorted for and was given after the aims and objectives of the study were explained to them.

Inclusion and Exclusion criteria: Subjects for this survey are only men who were apparently healthy and residents of South-South zone of Nigeria. However, subjects who are already diagnosed as been hypertensive and/or diabetic who are on medications were excluded from this study.

Data collection and analysis: The ages of the subjects were recorded and using standard procedures, their weights (Kg) and heights (M) were obtained and BMI determined.

Also, blood samples were collected for the analysis of serum levels of MDA, antioxidant vitamin A and E based on standard methods.

Vitamin A and E were analyzed using the vitamin A and E high pressure liquid chromatography kits from America laboratory company (Alpco) diagnostics, USA. The principle is based on the flow of a mobile phase (liquid) containing the sample promoting the separation of sample components, which are differently distributed between this phase and a stationary phase.

Malondialdehyde (MDA) estimation was analyzed using the spectrophotometry method as described by Moore and Roberts [27]. The principle for MDA determination, a thiobarbituric reactive substance (TBARS) condenses with two equivalents of thiobarbituric acid to give a fluorescent red derivative that can be assayed spectrophotometrically.

Data Analysis: Done using SPSS (version 17), the data obtained were analyzed and the means compared using the student t test with significant level taking at $p<0.05$.

Results

There were 200 adult male who took part in the study. The WHO reference for body mass index was used to classify subjects into three subgroups namely under-weight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2) and over weight (25-29.9 kg/m^2) and consisted of 60, 80 and 60 subjects respectively.

The results showed that as age (years) progresses, MDA level increases while vitamin A and E levels decrease (table 1). Although variabilities were observed in the different age groups in term of the mean MDA and vitamin A levels, statistically, the differences between the different ages were not significantly different ($p>0.05$). Comparatively however, mean vitamin E level for the subjects between the ages of 36 and 40 (3.01) was significantly lower ($p<0.05$) compared to the mean vitamin E level of subjects between 18 and 20 years (9.85). On the association between age and MDA and antioxidants, it was observed that age (in years) correlates positively with MDA (+0.81) but correlates negatively with vitamin E (-0.77) and A (-0.62) (see figure 1).

Table 1: Age distribution of the mean MDA and antioxidants levels of the subjects

Parameters	Ages in years				
	18-20 (n=41)	21-25 (n=58)	26-30 (n=45)	31-35 (n=34)	36-40 (n=22)
MDA(nmol/ml)	2.31	2.49	3.02	3.21	3.41
Vitamin A (mg/l)	0.43	0.39	0.32	0.28	0.23
Vitamin E (mg/l)	9.85	8.2	6.15	5.02	3.01*

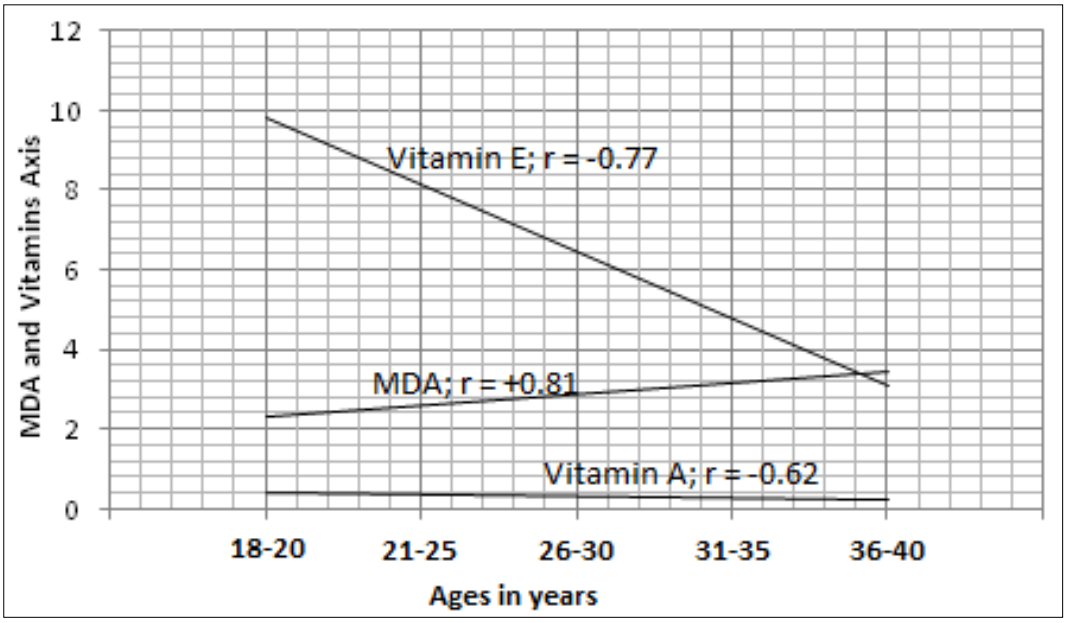

Fig 1: Relationship between Age (in years) and MDA and antioxidant vitamins of the subjects.

Body weight was observed to vary with MDA and antioxidants levels (table 2). While increasing body weight increases MDA level, increasing body weight reduces vitamin A and E levels. The overweight subjects have the highest MDA level (5.77) but the lowest antioxidants levels (0.41 for vitamin A and 9.73 for vitamin E) compared to subjects who are normal weight or underweight. However, the differences were not significantly different ($p>0.05$) compared between the groups. On the association between body weight and MDA and antioxidants, it was observed that body weight (in Kg/M^2) correlates positively with MDA (+0.89) but correlates negatively with vitamin E (-0.82) and A (-0.82) (see figure 2).

Table 2: Body weight distribution of the mean MDA and antioxidants levels of the subjects.

Parameters	Body weight in Kg/M^2		
	Under-weight (n=60)	Normal weight (n=80)	Over weight (n=60)
MDA (nmol/ml)	4.17	4.5	5.77
Vitamin A (mg/l)	0.63	0.61	0.41
Vitamin E (mg/l)	11.33	11.17	9.73

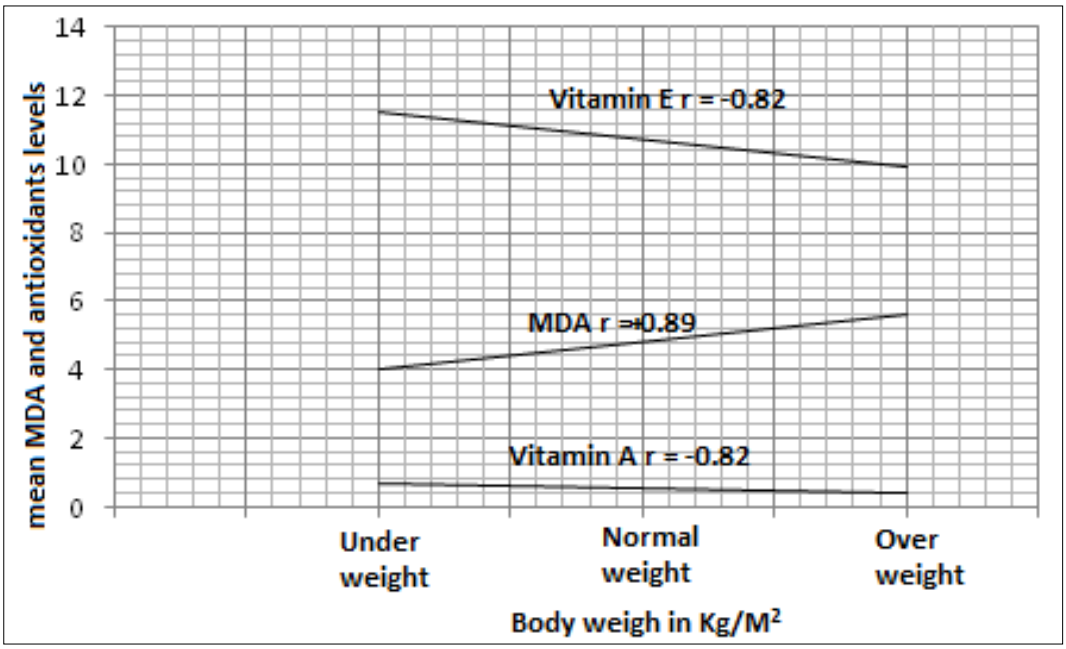

Fig 2: Relationship between body weight (in Kg/M^2) and MDA and antioxidant vitamins of the subjects.

Discussion

This study showed that oxidative stress indicated by MDA is increased while antioxidants status is decreased as age progresses. In agreement with the findings of this study, many studies have reported increased oxidative damage in cells associated with aging [28, 29, 30].In support of this finding,

increased ROS production by mitochondria and increased 8-oxo-dG content in the mt-DNA are frequently detected in aged tissues [31, 32,33,34,35] This therefore indicates that the aging process is a contributory factor to the increased accumulation of oxidative stress pointers; which based on the present study are the increased MDA level and reduced antioxidant vitamin levels here in studied. According to Sena and Chandel[36] and Janssen-Heininger*et al*., [37] basal levels of ROS/RNS are indispensible for redox signaling and cell survival; however, high levels of ROS/RNS would be detrimental to cells and have been thought to contribute to aging and the pathogenesis of numerous aging-related diseases [36, 38]. Hence, the increased MDA and reduced vitamin A and E levels observed in the present study as age progresses are justified.

Also, this study showed that increasing body mass is associated with increase oxidative stress which was revealed in this study by the increased MDA level and decreased antioxidants status. In agreement with this finding, a number of studies have provided direct evidence of mitochondrial dysfunction associated with obesity, related to increased ROS production, supporting the development of insulin resistance [39]. In addition, systemic oxidative stress is part of the numerous biological alterations reported during chronic obesity [40]. Additionally, in agreement with the finding of this study, adipocytes isolated from mice fed with high-fat diet [41] or exposed to nutrient excess in vivo [42] demonstrated significantly elevated ROS in vitro. Evidences regarding obesity-induced oxidative stress are derived from several clinical studies, which have established correlations of biomarkers, or end-products of free radicals-mediated oxidative stress such as lipid peroxidation or protein-carbonylation products, with body mass index [43, 44].To determine whether fat accumulation is primarily involved in increased oxidative stress-associated obesity, a study analyzed lipid peroxidation and H2O2 production in adipose tissues from obese KKAy mice and found a specific elevation of lipid peroxidation and H2O2 production in WAT from these obese rodents, but not in liver, muscles, or aorta[45] and this has been confirmed in other models of obesity such as high-fat diet [46] or ob/ob mice [47].

The deteriorating impact on antioxidant vitamin A and E by increasing age and body weight presented in this study may also have contributed to the worsen MDA level considering that antioxidant system is important in neutralizing the action of reactive substances. In accordance with the finding of this study, obese individual has been shown to generally have a relatively low total antioxidant status (TAS) characterized by lower levels of serum vitamins A, E, C, and β-carotene as well as glutathione [48, 49] and with increased oxidative stress [50]. Although adipose tissue storage generally equilibrates with circulating levels of molecules [51,52], fat can also act as sink concentrating vitamins in adipocyte lipid droplets therefore limiting their bioavailability [53,54]. Silencing of the antioxidant enzyme glutathione-S-transferase (GSTA4) in cultured adipocytes or its invalidation in mice and human have been reported to results in increased ROS production and mitochondrial dysfunction [46]. Specifically, a decrease in expression and activities of antioxidant enzymes such as SOD, GPX, or catalase have been reported in WAT from obese mice models [45].

Conclusion

This study showed that age and increasing body weight positively correlates with MDA level but negatively correlates with antioxidant levels. In another words, as age and body mass increase, MDA level increase while antioxidant levels decrease in male individual. The findings in this study may be related to the age-related or age induction of diseases or the increase incidence and prevalence of diseases in individual with increasing weight and obese state. It is therefore recommended that similar study be conducted among female to see the effect of sex hormones on our findings.

References

1. Watson J. Oxidants, antioxidants and the current incurability of metastatic cancers. Open Biol.2013; 3:120-144.
2. Knoefler D, Thamsen M, Koniczek M, Niemuth NJ,Diederich AK, Jakob U. Quantitative in vivo redox sensors uncover oxidative stress as an early event in life.Mol. Cell. 2012; 47:767-776
3. Groeger G, Doonan F, Cotter TG, Donovan M. Reactive oxygen species regulate prosurvival ERK1/2 signaling and bFGF expression in gliosis within the retina. Invest. Ophthalmol. Vis. Sci.2012; 53:6645-6654.
4. Bevilacqua E, Gomes SZ, Lorenzon AR, Hoshida MS,Amarante-Paffaro AM.NADPH oxidase as an important source of reactive oxygen species at the mouse maternal-fetal interface: putative biological roles. *R*eprod. Biomed.2012; 25:31-43.
5. Groeger G, Quiney C, Cotter TG. Hydrogen peroxide as a cell-survival signaling molecule. Antioxid. Redox Signaling. 2009; 11:2655-2671.
6. Mandelker L. Introduction to oxidative stress and mitochondrial dysfunction. Vet. Clin. North. Am. Small. Anim. Pract.2008; 38:1-30.
7. Sies H. Oxidative stress: Introductory remarks. In: Sies H (ed.). Oxidative Stress. Amsterdan: Academic Press. 1985,1-7.
8. Halliwell B. Antioxidants in human health diseases. Annu Rev Nutr.1996; 16:33-50.
9. Halliwell B,Gutteridge JM. Free radicals in biology and medicine. Oxford: Oxford University Press. 1989.
10. Harman D. Aging: a theory based on free radical and radiation chemistry.Journal of Gerontology.1956; 11(3):298-300.
11. Grant CM. Metabolic reconfiguration is a regulated response to oxidative stress.J Biol. 2008; 7:1.
12. Poli G, Schaur RJ, Siems WG, Leonarduzzi G. 4-Hydroxynonenal: A membrane lipid oxidation product of medicinal interest. Med Res Rev. 2008; 28:569-631.
13. Ramos LR. Fatoresdeterminantes do envelhecimentosaudávelemidososresidentesemcentrourbano: ProjetoEpidoso, São Paulo. Cad SaúdePública. 2003; 19:793-8.
14. Hayflick L. How and why we age. Experimental Gerontology. 1998; 33(7-8):639-653.
15. Kirkwood TBL. Understanding the odd science of aging. Cell.2005; 120(4):437-447.
16. Hedley AA, Ogden CL, Johnson CL, Carroll MD, CurtinLR, Flegal KM. Prevalence of overweight and

obesity among US children, adolescents, and adults, 1999-2002. JAMA. 2004; 291:2847-50.
17. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. JAMA. 2002; 288:1723-7.
18. Mokdad AH, Bowman BA, Ford ES, Vinicor F, MarksJS, Koplan JP. The continuing epidemics of obesity and diabetes in the United States. JAMA. 2001; 286:1195-200.
19. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: prevalence and trends, 1960–1994. Int J ObesRelatMetabDisord. 1998; 22:39-47.
20. Kuskowska-Wolk A, Rossner S. Body mass distribution of a representative adult population in Sweden. Diabetes Res ClinPract. 1990; 10(suppl):S37-S41.
21. Manson JE, Willett WC, Stampfer MJ. Body weight and mortality among women. N Engl J Med. 1995; 333:677-85.
22. Fogelholm M, Kujala U, Kaprio J, Sarna S. Predictors of weight change in middle-aged and old men. Obes Res. 2000; 8:367-73.
23. Grinker JA, Tucker K, Vokonas PS, Rush D. Body habitus changes among adult males from the normative aging study: relations to aging, smoking history and alcohol intake. Obes Res. 1995; 3:435-46.
24. Rissanen A, Heliovaara M, Aromaa A. Overweight and anthropometric changes in adulthood: a prospective study of 17,000 Finns. Int J Obes. 1988; 12:391-401.
25. Kannel WB, Gordon T, Castelli WP. Obesity, lipids, and glucose intolerance. The Framingham Study. Am J ClinNutr. 1979;32:1238-45.
26. World Medical Association (WMA) Declaration of Helsinki-Ethical Principles for Medical Research involving human subjects. 2000. http://www.wma.net/e/ethicsunit/helsinki.htmassessed 6th October, 2014.
27. Moore K, Roberts LJ. Measurement of lipid peroxidation.Free Radical Research.1998; 28:659-671.
28. Hamilton ML, Van Remmen H, Drake JA. Does oxidative damage to DNA increase with age? Proceedings of the National Academy of Sciences of the United States of America. 2001; 98(18):10469-10474.
29. Fraga CG, Shigenaga MK, Park JW, Degan P, Ames BN. Oxidative damage to DNA during aging: 8-Hydroxy-2'-deoxyguanosine in rat organ DNA and urine," Proceedings of the National Academy of Sciences of the United States of America. 1990; 87(12):4533-4537.
30. Oliver CN, Ahn BW,Moerman EJ. Age-related changes in oxidized proteins. Journal of Biological Chemistry. 1987; 262(12):5488-5491.
31. Maynard S, Schurman HS, Harboe C, de Souza-PintoCN,Bohr AV. Base excision repair of oxidative DNA damage and association with cancer and aging. Carcinogenesis. 2009; 30(1):2-10.
32. Capel F, Rimbert V, Lioger D. Due to reverse electron transfer, mitochondrial H2O2 release increases with age in human vastuslateralis muscle although oxidative capacity is preserved. Mechanisms of Ageing and Development. 2005; 126(4):505-511.
33. Sohal RS, Dubey A. Mitochondrial oxidative damage, hydrogen peroxide release, and aging. Free Radical Biology and Medicine.1994; 16(5):621-626.
34. Sohal RS,Sohal BH. Hydrogen peroxide release by mitochondria increases during aging. Mechanisms of Ageing and Development.1991; 57(2):187-202.
35. Sawada M, Carlson JC. Changes in superoxide radical and lipid peroxide formation in the brain, heart and liver during the lifetime of the rat. Mechanisms of Ageing and Development. 1987; 41(1-2):125-137.
36. Sena LA, Chandel NS. Physiological roles of mitochondrial reactive oxygen species. Mol. Cell. 2012; 48:158-167.
37. Janssen-Heininger YM, Mossman BT, Heintz NH,Forman HJ, Kalyanaraman B, Finkel T*et al*. A. Redox-based regulation of signal transduction: principles, pitfalls, and promises. Free Radical Biol. Med. 2008; 45:1-17.
38. Malinin NL, West XZ, Byzova TV. Oxidation as the stress of life Aging (Albany NY). 2011; 3:906-910.
39. De Pauw A, Tejerina S, Raes M, Keijer J,Arnould T.Mitochondrial (dys)function in adipocyte (de)differentiationand systemic metabolic alterations. American Journal of Pathology.2009; 175(3):927-939.
40. Roberts CK, Sindhu KK. Oxidative stress and metabolic syndrome. Life Sciences. 2009; 84(21-22):705-712.
41. Talior I, Tennenbaum T, Kuroki T,Eldar-Finkelman H. PKC-δ-dependent activation of oxidative stress in adipocytes of obese and insulin-resistant mice: Role for NADPH oxidase. American Journal of Physiology: Endocrinology and Metabolism.2005; 288(2):E405-E411.
42. Lin Y, Berg HA, Iyengar P.The hyperglycemia-induced inflammatory response in adipocytes: the role of reactive oxygen species. Journal of Biological Chemistry.2005; 280(6):4617-4626.
43. Sankhla M, Sharma TK, Mathur K. Relationship of oxidative stress with obesity and its role in obesity induced metabolic syndrome. Clinical Laboratory. 2012; 58(5-6):385-392.
44. Vincent HK, Taylor AG. Biomarkers and potential mechanisms of obesity-induced oxidant stress in humans. International Journal of Obesity.2006; 30(3):400-418.
45. Furukawa S, Fujita T, Shimabukuro M. Increased oxidative stress in obesity and its impact on metabolic syndrome. Journal of Clinical Investigation. 2004;114(12):1752-1761.
46. Curtis JM, Grimsrud PA, Wright WS. Down-regulation of adipose glutathione S-tansferase A4 leads to increased protein carbonylation, oxidative stress, and mitochondrial dysfunction. Diabetes.2010; 59(5):1132-1142.
47. Houstis N, Rosen ED, Lander ES. Reactive oxygen species have a causal role in multiple forms of insulin resistance. Nature. 2006;440(7086):944-948.
48. Neuhouser ML, Rock CL, Eldridge AL. Serum concentrations of retinol, α-tocopherol and the carotenoids are influenced by diet, race and obesity in a sample of healthy adolescents. Journal of Nutrition.2001; 131(8):2184-2191.
49. Kuno T, Hozumi M, Morinobu T, Murata T, Mingci Z, Tamai H. Antioxidant vitamin levels in plasma and low

density lipoprotein of obese girls. Free Radical Research. 1998; 28(1):81-86.
50. Ramos FL, Shintani A, Alp Ikizler T,Himmelfarb J. Oxidative Stress and Inflammation Are Associated with Adiposity in Moderate to Severe CKD. Journal of the American Society of Nephrology.2008;19(3):593-599.
51. Blum M, Dolnikowski G, Seyoum E. Vitamin D 3 in fat tissue. Endocrine.2008;33(1):90-94.
52. Parker RS. Carotenoids in human blood and tissues. Journal of Nutrition.1989; 119(1):101-104.
53. Galinier A, Carrière A, Fernandez Y. Adipose tissue proadipogenic redox changes in obesity. The Journal of Biological Chemistry. 2006; 281(18):12682-12687.
54. Traber GM, Kayden JH. Tocopherol distribution and intracellular localization in human adipose tissue. American Journal of Clinical Nutrition.1987; 46(3):488-495.