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Lipid Peroxidation and lipid Profile in Hypertensive Patients in Sokoto, Nigeria

[1]U, Wali, [1]A.A. Binji, [2]K. Ahmad and [3]A. Usman
[1]Dept. of Chemical Pathology, School of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto
[2]Dept. of Biochemistry, Usmanu Danfodiyo University, Sokoto Nigeria
[3]Dept. of Chemistry, Umaru Musa Yar'adua University, Katsina – Nigeria
[*Corresponding Author: E-Mail: Usmanwali90@yahoo.com; ☎: +234(0)8032845258]

ABSTRACT: Hypertension and dyslipidaemia are associated with oxidative stress and are major causes of cardiovascular disease amounting to 30% of global death rate. In the current work, malondialdehyde and lipid profile were estimated in sixty hypertensive patients attending outpatient clinic of the Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria and the results compared with those of apparently healthy non-hypertensive volunteers of comparable age and social status. Serum levels of MDA, TC, TG, LDL-C, VLDL-C and AIX in hypertensive subjects were 122.80 ± 14.66, 6.99 ± 0.59, 2.49 ± 0.23, 3.68 ± 0.63, 1.14 ± 0.23 and 2.02 ± 0.65 mmol/l respectively while in non hypertensive subjects the results were 60.14 ± 11.20, 5.31 ± 0.89, 1.79 ± 0.65, 0.71 ± 0.52, 0.83 ± 0.32 and 0.21 ± 0.19 mmol/l respectively. There were significantly ($P < 0.05$) higher levels in hypertensives. The serum HDL-C was significantly ($p < 0.05$) lower in hypertensives (2.29 ± 0.41 mmol/l) than in non-hypertensives (3.89 ± 0.76 mmol/l) subjects respectively. There were higher incidences (71%) of lipid peroxidation and dyslipidaemia in the hypertensives. The results suggest that hypertensives in the study area have high serum levels of MDA and lipid profile, an indication that the hypertensives are predisposed to increased oxidative onslaught.
Keywords: Hypertensive, malondialdehyde, dyslipidaemia, lipid profile.

INTRODUCTION

Cardiovascular diseases include hypertension, coronary heart disease, cerebrovascular disease, peripheral artery disease, congenital heart disease and rheumatic heart disease (Kumar *et al.*, 2004). Hypertension is a sustained elevation of systemic arterial pressure to a level greater than or equal to 140mmHg systolic and 90mmHg diastolic in an individual aged 15 years or above (Mc Gowan and Chopra, 2001). It continues to be a major cardiovascular risk factor and is now regarded as a major public health problem (Murray and Lopez, 1997).

Cardiovascular disease accounts for one-third of global deaths and a major contributor to the global disease burden (WHO, 2002). World Health Organisation (2002) estimated an increase in the number of disability and death from cardiovascular disease to 8.1 and 7.9 million in 2010 for men and women respectively. It accounts to 9.2% of total deaths in the African region (WHO, 2002). Hypertension is implicated in 35% of all atherosclerotic cardiovascular events (Kannel, 1996), including 49% of all cases of heart failure (Kannel, 1996). The major cause of stroke is

hypertension (83.9%) (Njoku and Adeloju, 2004). In Nigeria stroke is the major cause of neurological admission and its incidence may be on the increase (Njoku and Adeloju, 2004).

Hypertension and other cardiovascular diseases rank among the leading causes of mortality in industrialized nations (Stekelings *et al.*, 2007). Accumulating evidence suggest that seven million people die of hypertension every year globally and 1.5 billion suffer dangerous diseases every year due to high blood pressure (Kadiri, 2005).The prevalence of hypertension globally as at 2000 was 26.4% of adult population and projected to reach 29.2% by the year 2025 (Kadiri, 2005). In Nigeria, it is estimated that 20% of the adult population have hypertension (Khosh and Khosh, 2001). It is one of the leading causes of death and disability due to complications such as coronary heart disease, stroke, congestive heart disease, end-stage renal disease and peripheral vascular disease (Khosh and Khosh, 2001).

Propagative lipid peroxidation is a degenerative process that affects cell membranes and other lipid containing structures under conditions of oxidative

stress (Halliwell and Gutteridge, 1990). Oxidation of LDL resulting from increased oxidative stress is an essential early event in the pathogenesis of atherosclerosis (Halliwell and Gutteridge, 1990). Atherosclerosis is a major complication of hypertension (Halliwell and Gutteridge, 1990). Hypertension is associated with an increased presence of free radicals and therefore elevated oxidative stress of the human body (Packer *et al.*, 2000).

Many risk factors are associated with cardiovascular diseases one of which is abnormal level of serum cholesterol. High blood cholesterol has been shown to be a leading cause of cardiovascular disease (Murry *et al.*, 1993). High level of LDL-C may directly impair endothelial cell function through increased production of free radicals that deactivate nitric oxide. LDL accumulates within the intima at the site of increased endothelial permeability (Murry *et al.*, 1993). The chemical changes of lipid induced by free radicals generated in macrophages or endothelial cells in the arterial wall yield oxidized LDL-C which is ingested by macrophages through scavengers receptor distinct from LDL receptor, thus forming form cells (Murry *et al.*, 1993; Kumar *et al.*,2004). Oxidized LDL also increases monocytes accumulation in lesion and stimulates release of growth factors and cytokines (Murry *et al.*, 1993; Kumar *et al.*, 2004). Growth factors stimulate release of growth factors and cytokines (Murry *et al.*, 1993; Kumar *et al.*, 2004). Growth factors stimulate migration and proliferation of smooth muscle cells from the media into the intima thereby converting fatty streak into a mature fibrofatty atheroma and contribute to the progressive growth of atherosclerotic lesion, the underlying cause of cardiovascular disease (Murry *et al.*, 1993; Kumar *et al.*, 2004).

Production of Reactive oxygen species (ROS contributes to the dysregulation of physiological processes which leads to structural and functional alteration observed in hypertension and atherosclerosis (Dhalla *et al.*, 2000). Thus, controlling hypertension may greatly reduce the risk of disability and death from cardiovascular disease.

In this study, serum malondialdehyde, total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol and AIX were estimated in hypertensives and the results compared with those of apparently healthy non-hypertensives of comparable socio-economic status.

MATERIALS AND METHODS
Subjects
The subjects employed for this study were sixty (60) hypertensive patients of both sexes who were attending the medical outpatient clinic of the Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. Also,sixty (60) apparently healthy subjects of both sexes were recruited to serve as control. The consents of all the subjects were sought for and obtained. Ethical committee approval was obtained from Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria.

Blood samples
Fasting blood samples were collected by venipuncture and delivered into clean dry tubes and allowed to clot at room temperature. The samples were centrifuged at 3000 rpm for 5 minutes using desktop centrifuge and the serum separated and kept in labelled sample bottles at -20°C until required.

Reagents
All the reagents used for the study were of analytical grade. Malondialdehyde kit was obtained from Northwest Life Science Specialist, Vancouver, Canada. Kits for the assay of total cholesterol, triglyceride, and HDL-cholesterol were obtained from Randox laboratories, Switzerland.

Analytical Methods
Serum malondialdehyde was estimated using Thiobarbituric Acid Reactive Substance (TBARS) method of (Wong *et al.*, 1987). Total cholesterol level was determined by CHOD-PAP method of (Richmond, 1972). Triglyceride level was determined by GPO-PAP reaction method of(Bucola and David 1973). HDL-cholesterol was determined by CHOD-PAP reaction method of(Burstein *et al.*, 1980). LDL-Cholesterol and VLDL-cholesterol were calculated using Friedewald formula (Friedewald *et al.*, 1974). Atherogenic index (AIX) was calculated as the ratio of LDL-C to HDL-C according to Glueck and Segal, (1986).

Statistical Analysis

Results are presented as mean ± standard deviation and separated on the basis of gender. Significant differences in mean at 5% level were determined using ANOVA.

RESULTS AND DISCUSSION

The results of the current work show significant difference (P<0.05) between serum MDA of the hypertensive and non-hypertensives. Serum levels of TC, TG, LDL-C, VLDL-C and AIX were significantly higher (P<0.05) in hypertensives than in the non-hypertensives (Table 1). HDL-C was significantly lower (P<0.05) in hypertensive than in non-hypertensive. Gender appears not to have significant effect (P>0.05) on the serum levels of MDA and lipid profile (Table 1).

Essential hypertension is characterized by elevated level of oxidative stress indices and lipid abnormalities due to lipid peroxidation (Lawrence, 2010). Lipid profile has been reported to be the important predictor for metabolic disturbances including hypertension, dyslipidaemia, diabetes, hyperinsulinaemia and cardiovascular diseases (Lawrence, 2010). Cholesterol serves as a major constituent of atheromatous plaque, and many epidemiological studies show strong relationship between plasma cholesterol concentration and the prevalence of coronary heart disease (Lawrence, 2010). The increased AIX in hypertensive may suggest disruption of membrane fluidity and lead to membrane alteration of function (Rieler, 1995). This could be linked to the deleterious actions of ROS in which case the membrane lipids succumb easily (Rieler, 1995). Increased LDL-C level in the hypertensives aggravates the disease due to the role the LDL particle has in transporting cholesterol from the liver cells to body cells, so that atherosclerosis and heart attack may result (Rieler,1995). Increased oxidative stress also occurs because oxidized LDL particles inactivate NO and aggrevates hypertension (Tomasi *et al.,* 2003).

Decreased HDL-C is a risk factor of atherosclerosis and heart attack because the HDL particles transport cholesterol from body cells to the liver for productive purposes (Lawrence, 2010). Hypertensive patients develop atherosclerotic vascular disease earlier and with greater severity than non-hypertensive subjects (Ceriello and Motz, 2004). Free oxygen radicals are one of the factors, which participate via lipid peroxides in the development of atherosclerosis (Ceriello and Motz, 2004). Increased lipid peroxidation in hypertensives is due to an altered intracellular ratio between free radicals and antioxidant systems (Ceriello and Motz, 2004). The imbalance between free radical production and antioxidant capacity leads to oxidative stress, which in turn is associated with the development of cardiovascular disease (Bilbis, 2008). Most of the hypertensives (71%) show lipid peroxidation and dyslipidaemia. Hypertension and dyslipidaemia are associated with oxidative stress and are major causes of cardiovascular diseases (Ceriello and Motz, 2004). According to Ahmad *et al.,* (2011) hypertensive subjects are characterized by increased total cholesterol, LDL-C and decreased HDL-C due to decreased antioxidant vitamins and minerals. Hypertensives have elevated levels of free radicals and lower levels of antioxidants (Schneider *et al.,* 2000).

Table 1: Serum MDA and Lipid Profile of Hypertensive in Sokoto, Nigeria

Parameters	Hypertensives			Controls		
	Male	Female	Total	Male	Female	Total
N	32	28	60	32	28	60
MDA (nmol/ml)*	113.20±29.58[a]	138.77±24.66[a]	122.80±14.66[a]	67.63±14.89	51.59±12.86	60.14±11.2
TC (mmol/l)*	6.86±0.93[a]	7.13±1.47[a]	6.99±0.59[a]	5.33±0.84	5.39±0.76	5.31±0.89
TG (mmol/l)*	2.43±0.36[a]	2.56±0.59[a]	2.49±0.54[a]	1.83±0.54	1.75±0.77	1.79±0.65
HDL-C (mmol/l)*	1.97±0.53[a]	2.45±0.72[a]	2.29±0.41[a]	3.81±0.87	3.78±0.61	3.89±0.76
LDL-C (mmol/l)*	3.80±1.07[a]	3.53±1.52[a]	3.68±0.63[a]	0.67±0.55	0.74±0.49	0.71±0.52
VLDL-C (mmol/l)*	1.14±0.24[a]	1.14±0.19[a]	1.14±0.23[a]	0.85±0.27	0.81±0.37	0.83±0.32
AIX*	2.19±1.16[a]	1.82±1.89[a]	2.02±0.65[a]	0.21±0.22	0.20±0.14	0.21±0.19

*Values bearing asterisk differ significantly ($P<0.05$) using ANOVA. a =superscript for comparing horizontally.
Values differ significantly from the respective control

Table 2: Prevalence of Lipid Peroxidation and Dyslipidaemia in Hypertensives in Sokoto, Nigeria

Parameters	Male	Female	Total **	Reference Range*
MDA (nmol/ml)	84.38	89.29	86.67	39.50-110.00
TC (mmol/l)	81.25	75.00	78.33	3.90-6.40
TG (mmol/l)	65.63	71.43	68.33	0.54-2.44
HDL-C (mmol/l)	96.88	89.29	93.33	2.40-4.73
LDL-C (mmol/l)	84.38	28.57	60.00	0.12-2.77
VLDL-C (mmol/l)	40.63	57.14	48.33	0.20-1.22
AIX	84.38	57.14	71.67	0.03-1.20

*Serum levels of MDA and lipid profile for non-hypertensive subjects were used for deciding the normal range in the study area.
**Total is pooled values for both the male and female subjects.

CONCLUSION
Based on the results of the current study therefore, it can be concluded that hypertensives in the study area have high serum levels of MDA and lipid profile, an indication that the hypertensives are predisposed to increased oxidative onslaught.

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