Journal of Medical Sciences

ISSN 1682-4474

science alert

ANSInet
an open access publisher
http://ansinet.com

Research Paper

J. Med. Sci., 8 (8): 691-698
15th December, 2008

Lipid Profile and Lipid Peroxidation among Ghanaian Pregnancy-Induced Hypertensives

[1]L. Ahenkorah, [1]W.K.B.A. Owiredu, [1]E.F. Laing, [1]N. Amidu and [2]C.A. Turpin

This study was aimed at investigating oxidative stress among Ghanaian women with Pregnancy-Induced Hypertension (PIH). One hundred Pregnancy-Induced Hypertension women: Thirty with preeclampsia, seventy with gestational hypertension and fifty normotensive pregnant women (controls) in the second half of pregnancy were recruited for this study. There was a significant increase in triglycerides and LDL-cholesterol in the subject groups compared to the control. Malondialdehyde (MDA), the lipid peroxidation marker among the PIH subjects was significantly increased as compared to the normotensive pregnant women (controls). A significant positive correlation between MDA and blood pressure (Systolic and Diastolic blood pressure) was also observed. This study clearly indicates that Ghanaian women presenting with PIH are very prone to dyslipidemia as well as lipid peroxidation, this might in part explain the oxidative stress and endothelial vascular dysfunction observed in these group of women.

Key words: Pregnancy, induced hypertension, malondialdehyde, normotensive pregnant women, oxidative stress, anthropometric data

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

For further information about this article or if you need reprints, please contact:

Dr. William K.B.A. Owiredu
Department of Molecular Medicine, KNUST, Kumasi, Ghana

Tel: +233 244 228 667

ANSInet
Asian Network for Scientific Information

[1]Department of Molecular Medicine, School of Medical Sciences,
[2]Department of Obstetrics and Gynaecology, School of Medical Sciences/Komfo Anokye Teaching Hospital, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

INTRODUCTION

Pregnancy-Induced Hypertension (PIH) continues to be a major obstetric problem in present-day healthcare practice. It presents a great medical dilemma because it affects not only maternal health but also puts foetal development at risk. Worldwide, the hypertensive disorders of pregnancy are very common and are responsible for 12% of maternal mortality during pregnancy and the puerperium (Bellany *et al*., 2007). Preeclampsia is the leading cause of maternal mortality in developed countries and is associated with a five-fold increase in perinatal mortality; the major cause of foetal compromise is reduced uteroplacental perfusion (Hubel, 1999). In Ghana, an alarming 40% of maternal deaths are as a result of hypertensive pregnancy, antepartum haemorrhage and post partum haemorrhage (Osei-Nketiah, 2001).

Gestational Hypertension (GH) and preeclampsia (PE) (together referred to as PIH) are conditions of pregnancy characterized by increased blood pressure. Preeclampsia, according to the National High Blood Pressure Education Program of the USA (1990) is defined as hypertension developing after 20 weeks' gestation with proteinuria and/or oedema. Gestational hypertension on the other hand, is hypertension developing after 20 weeks' gestation without other signs of preeclampsia. Preeclampsia is a systemic disease characterized not only by hypertension but also by increased peripheral vascular resistance, diffuse endothelial dysfunction, proteinuria and coagulopathy (Solomon and Seely, 2001). In the absence of severe disease manifestations, discrimination between preeclampsia and gestational hypertension may be difficult but usually the distinction is often made solely on the basis of urine protein determination, frequently by dipstick protein measurement (Meyer *et al*., 1994).

In spite of varying attempts to comprehend the primary pathophysiology of PIH, no particular theory regarding its origin has been established yet and this limits the ability to prevent and treat this medical condition. Varying hypothesis have been put forward for this obstetric disorder, including immune, genetic, placental abnormalities (Seely and Solomon, 2003) and endothelial dysfunction (Roberts, 1998). Some pregnant women with PIH may also present with dyslipidemia (Belo *et al*., 2002; Sattar *et al*., 1997a). There is increasing evidence that endothelial cell dysfunction is the primary pathophysiological mechanism which causes preeclampsia (Friedman *et al*., 1991; Roberts *et al*., 1989). However, the pathway mediating endothelial cell layer dysfunction still remains unclear. One hypothesis receiving amplified attention is that the endothelial dysfunction may be the result of increased oxidative stress, which is characterized by disequilibrium between oxidant and antioxidant forces in favour of oxidation. The lipid peroxidation process, initiated by the reaction of free radicals with polyunsaturated fatty acids (Hubel *et al*., 1989) is used as a marker of oxidant force.

Lipid peroxidation is a reaction whereby molecular oxygen is incorporated into poly-unsaturated fatty acids (PUFA) to yield lipid peroxides. Lipid peroxidation mediated by free radicals is considered to be the major mechanism of cell membrane destruction and cell damage (endothelial damage) and is a key contributing factor to the pathophysiologic condition of preeclampsia (Ozan *et al*., 2002). Diverse studies world wide have reported elevated lipid levels in PIH patients (GH and PE) (Kaaja *et al*., 1995; Sattar *et al*., 1997a; Seely and Solomon, 2003; Forest *et al*., 2005; Turpin *et al*., 2008). Cell membranes are generally made up of lipid bilayers and thiol containing proteins. The unsaturated lipid component and thiol containing proteins of the cell membranes are susceptible to free radical attack. Antioxidants are compounds that dispose, scavenge and suppress the formation of free radicals, or oppose their actions (Sies, 1991). Free radicals are formed in both physiological and pathological conditions in mammalian tissues (Krishna Mohan and Venkataramana, 2007; Plaa and Witschi, 1976). But normally, defense mechanisms of the body play an important role in the form of antioxidants, making every effort to minimize the damage, as an adaptation to stressful situations. An increased disequilibrium between oxidants (free radicals) and antioxidants results in oxidative stress when the imbalance favours oxidation. The unrestrained production of free radicals is considered as an important factor in the tissue damage induced by several conditions (Sato *et al*., 1996) as reportedly observed in PIH patients (Mutlu-Turkoglu *et al*., 1998). There is considerable epidemiological, laboratory and clinical evidence to suggest a significant role for free radical activation and deficient or over utilized antioxidant defenses in the pathogenesis of PIH (Gulmezoglu *et al*., 1997). This current study, therefore, was aimed at investigating the possible link between the lipidaemic status, lipid peroxidation and oxidative stress in PIH women as compared to normotensive pregnant women.

MATERIALS AND METHODS

Subjects: This study was conducted at the Komfo Anokye Teaching Hospital in Kumasi, Ashanti Region of Ghana between November, 2006 and December, 2007 and was approved by the SMS/KATH Committee on Human Research Publications and Ethics (CHRPE/KNUST/KATH/15_03_08). Two groups of

women within the age group 17-45 years, comprising of one hundred pregnant women with Pregnancy-Induced Hypertension (seventy with gestational hypertension and thirty with preeclampsia) and fifty normotensive pregnant women with uncomplicated pregnancy visiting the Obstetrics and Gynaecology Department of the Hospital were recruited for the study. Most importantly, women with known renal disease, diabetes and hypertension prior to pregnancy or cardiovascular diseases were excluded from this study in both test and control. Smokers were also excluded from the study, since the constituents present in cigarette are potential sources of oxidative degradation of membrane lipids.

Pregnant women with normal blood pressure and without proteinuria were included in the control group. Eligible cases were pregnant women within the age range 17-45 years and who met the criteria of the National High Blood Pressure Education Program Working Group for PIH assessed by a single qualified Obstetrician/Gynaecologist. Briefly, the presence of high blood pressure on two occasions six hours apart was considered gestational hypertension while pregnant women who had proteinuria level of 2+ positive result on a dipstick, were considered as presenting with preeclampsia (Forest *et al*., 2005). All the subjects were Ghanaians and their participation was voluntary and informed consent was obtained from each of them.

Sample collection and preparation

Biochemical analysis: Fasting venous blood samples were drawn from the respondents between 7 am and 11 am. About 5 mL was drawn and dispensed into vacutainer® plain tubes which were then taken to the laboratory within an hour for centrifugation; the serum obtained was used for the biochemical assay. Biochemical assays on the serum were performed with the ATAC® 8000 Random Access Chemistry System (Elan Diagnostics, Smithfield, RI, USA). Parameters that were determined include: Total Cholesterol (TC), Triglycerides (TG), High density lipoprotein cholesterol (HDL-C), Low density lipoprotein cholesterol (LDL-C), Very low density lipoprotein cholesterol (VLDL-C). Serum LDL cholesterol (LDL-C) was calculated using the Frederickson-Friedewald's formula according to which LDL-C = TC - (HDL-C + VLDL-C). VLDL-C was calculated as 1/5 of triglycerides. Atherogenic index (AI) = [(total cholesterol-HDL cholesterol)/HDL cholesterol] (Schonfeld, 1979). The methods adopted by the automated instrument for the determination of the above parameters are according to the reagent manufacturer's instruction- JAS™ diagnostics, Inc. (JAS™ Diagnostics, Inc. Miami Florida, USA). Total Cholesterol Determination was determined according to the method described by Trinder (1969), Triglycerides determination employs a modified Trinder method (Trinder, 1969; Bartham and Trinder, 1972).

Low Density Lipoprotein cholesterol (LDL) determination: LDL was calculated according to Friedewald formula in accordance to the manufacturer's instructions.

$$LDL = TC - (HDL\text{-}C + VLDL)$$

Malondialdehyde (MDA) determination: MDA levels were determined by the MDA-Thiobarbituric acid (TBA) test which is the colorimetric reaction of MDA and TBA in acid solution. TBA reacted with MDA, a secondary product from lipid peroxidation, which generated an adduct of red colour, which was detected spectrophotometrically. This method is a fast, sensitive and low-cost method that can be used to indicate the extent of lipid peroxidation in a variety of systems (Shlafer and Shepard, 1984). The protocol used in this study is the (Kamal *et al*., 1989) modification of the (Shlafer and Shepard, 1984) protocol which is as follows:

About 0.5 mL of serum was treated with 2.5 mL of 20% trichloroacetic acid (TCA) and then 1 mL of 0.67% TBA. The mixture was incubated at 100°C for 30 min. After cooling, the sample was extracted with 4 mL n-butanol and centrifuged at 3000 rpm for 10 min. The absorbance of the supernatant was measured at 535 nm and the results were expressed as μmol L^{-1}, using the extinction coefficient of 1.56×105 L $mmol^{-1}$ cm.

Urinalysis: Early morning urine was collected in plastic containers from the respondents and urine protein was analyzed using the dip-stick qualitative method (CYBOW™ DFI Co Ltd., Gimhae-City, Republic of Korea).

Anthropometric variables

Measurements: Anthropometric measurements included height, measured without shoes and weight to nearest 0.1 kg in light clothing. Subjects were weighed on a bathroom scale (Zhongshan Camry Electronic Co. Ltd., Guangdong, China) and their height measured with a wall-mounted ruler. BMI was calculated by dividing weight (kg) by height squared (m^2).

Blood pressure: Blood pressure was taken by qualified obstetric nurses using a mercury sphygmomanometer and stethoscope. Measurements were taken from the left upper arm after subjects had been sitting for >5 min in accordance with the recommendation of the American Heart Association (Kirkendall *et al*., 1967). Triplicate measurements were taken with a 5 min rest interval between measurements and the mean value was recorded.

Statistical analysis: Values for the continuous variables are expressed as their Mean±SEM. Comparisons of the women with PIH (Gestational Hypertension and Preeclampsia separately and combined) against the control group were performed using unpaired students t-tests, a level of $p<0.05$ was considered as statistically significant. Comparison of clinical variables and blood lipid profiles between hypertensive and control groups was by Pearson Correlation Coefficient. Correlation was significant at the 0.05, 0.01 and 0.001 levels (2-tailed). GraphPad Prism version 5.00 for windows was used for statistical analysis (GraphPad software, San Diego California USA, www.graphpad.com).

RESULTS

Clinical data were collected from the PIH, PE, GH and control (CG) groups to characterize the study groups (Table 1). All the studied groups had similar mean age and mean pregnancy period. Indices of obesity (weight and BMI) were significantly increased in the entire studied group as compared to the control group. Mean SBP and DBP were significantly increased in PIH, PE and GH as was expected from the inclusion criteria. Proteinuria was also significantly increased when PIH and PE were compared to the control group.

From the lipid profile, plasma triglyceride and LDL-C levels were significantly higher in the various subject groups than in the controls, whereas the plasma HDL-C concentrations were much lower in these groups than in the control group, though it did not attain significant level. Total cholesterol, atherogenic index and VLDL concentrations were also not statistically different (Table 2). We have also calculated the ratios between different lipid fractions like LDL-C : HDL-C; TC : HDL-C; TG : HDL-C and HDL-C : VLDL-C. In the present study there was a significant rise in TG : HDL-C in the studied group as compared to control group.

The significant increase in the level of MDA in the various subject groups as compared to the control group was most pronounced when PE was compared to the control group (Fig. 1).

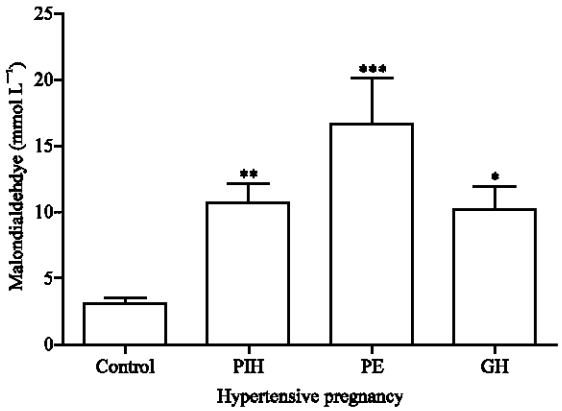

Fig. 1: Malondialdehdye levels in the various subject groups as compared to the control group. For Pregnancy-Induced Hypertension (PIH), n = 100, Preeclampsia (PE), n = 30, Gestational Hypertension (GH), n = 70, Control Group (CG), n = 50

Table 1: Clinical characteristics of PIH and normotensive pregnant women

Parameters	PIH	PE	GH	CG
Age (years)	31.81±0.60	30.37±1.29	31.43±0.65	30.22±0.57
GP (weeks)	30.40±0.83	30.67±0.96	29.43±0.72	31.00±0.85
Proteinuria (g L^{-1})	0.44±0.11**	1.43±0.30***	0.01±0.00	0.01±0.01
Weight (kg)	74.86±1.65*	76.43±2.75**	74.19±2.06*	68.86±1.32
BMI (kg m^{-2})	29.49±0.61*	30.11±0.91**	29.23±0.79*	27.05±0.48
SBP (mm Hg)	149.00±1.65***	133.80±4.25***	147.10±1.63***	105.80±1.54
DBP (mm Hg)	96.01±1.20***	98.08±1.76***	93.23±1.11***	65.29±1.07

Values are given as Means±SEM. Proteinuria values represent range. 0, 0.1, 0.3, 1 and 5 g L^{-1} corresponds to negative, trace, +, ++ and +++ in dipstick testing, respectively. ***$p<0.0001$, **$p<0.001$, *$p<0.05$ compared with normal pregnancy (Unpaired Student's t-test). For Pregnancy-Induced Hypertension (PIH), n = 100, Preeclampsia (PE), n =30, Gestational Hypertension (GH), n = 70, Control Group (CG), n = 50

Table 2: Blood lipids in normotensive pregnancy and PIH

Parameters	PIH	PE	GH	CG
Total cholesterol (mmol L^{-1})	6.43±0.17	6.32±0.30	6.10±0.19	6.41±0.22
Triglycerides (mmol L^{-1})	3.84±0.29*	3.43±0.19*	3.44±0.32*	2.54±0.26
HDL-cholesterol (mmol L^{-1})	1.98±0.06	1.88±0.11	1.98±0.07	1.99±0.08
VLDL-cholesterol (mmol L^{-1})	0.50±0.03	0.51±0.04	0.50±0.03	0.54±0.05
LDL-cholesterol (mmol L^{-1})	4.59±0.15*	4.44±0.20*	4.53±0.18*	3.84±0.19
Atherogenic index (mmol L^{-1})	2.24±0.40	2.37±0.23	2.08±0.57	2.22±0.16
LDL-C/HDL-C ratio	2.31±0.09	2.36±0.15	2.28±0.11	2.12±0.13
TC/HDL-C ratio	3.25±0.11	3.35±0.23	3.00±0.12	3.22±0.17
TG/HDL-C ratio	1.94±0.09*	1.83±0.16*	1.74±0.11*	1.27±0.16
HDL-C/VLDL-C ratio	3.95±0.37	3.68±0.51	3.94±0.49	3.69±0.37

Atherogenic index = [(total cholesterol-HDL cholesterol)/HDL cholesterol]. For Pregnancy-Induced Hypertension (PIH), n = 100, Preeclampsia (PE), n = 30, Gestational Hypertension (GH), n = 70, Control Group (CG), n = 50

Table 3: Pearson correlation co-efficient between clinical variables and lipid profile for PIH (Lower left-hand side) and CG (Upper right-hand side)

Parameters	AGE	SBP	DBP	GA	WT	BMI	TC	HDL	TG	LDL	VLDL	AI	MDA
AGE		-0.22	-0.11	-0.04	0.00	-0.01	0.06	0.08	-0.02	0.02	-0.02	-0.16	-0.71*
SBP	0.00		0.77***	-0.11	0.29	0.34*	0.04	0.06	-0.04	0.01	-0.04	0.01	-0.24
DBP	-0.10	0.42***		0.06	0.34*	0.35*	-0.04	0.15	0.02	-0.05	0.02	-0.06	-0.20
GA	-0.06	0.01	0.16		0.18	0.38**	0.18	-0.09	0.33*	0.14	0.33*	0.29	-0.26
WT	0.22*	-0.07	-0.06	0.04		0.77***	0.04	-0.03	0.26	0.00	0.26	0.11	0.22
BMI	0.19	-0.05	-0.02	0.10	0.91***		0.07	-0.10	0.43**	0.01	0.43**	0.18	0.30
TC	-0.05	-0.09	0.04	0.08	-0.03	0.02		-0.17	-0.13	0.94***	-0.13	0.47***	-0.05
HDL	-0.04	-0.09	-0.02	0.07	-0.15	-0.11	0.51***		-0.27	-0.41**	-0.27	-0.85***	0.24
TG	-0.01	-0.13	0.07	0.10	-0.03	0.01	0.94***	0.53***		-0.21	0.99***	0.29	0.28
LDL	-0.10	0.10	-0.05	-0.05	0.05	0.08	0.21*	-0.33***	-0.12		-0.21	0.62***	-0.17
VLDL	-0.20*	0.18	0.29**	-0.09	-0.23	-0.23*	-0.01	0.02	-0.02	0.02		0.29	0.29
AI	0.08	-0.03	-0.02	0.09	-0.10	-0.07	0.33***	0.62***	0.45***	-0.47***	0.04		-0.28
MDA	0.01	0.33*	0.36**	0.10	-0.13	-0.02	0.02	0.12	0.08	-0.13	0.12	0.14	

*Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed), ***Correlation is significant at the 0.001 level (2-tailed). SBP: Systolic blood pressure, DBP: Diastolic Blood Pressure, BMI: Body Mass Index, TC: Total serum cholesterol, GA: Gestation age, WT: Weight, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, VLDL: Very Low Density Lipoprotein, AI: Atherogenic Index, MDA: Malondialdehyde

Table 4: Pearson correlation coefficients between clinical variables and lipid profile for PE (Lower left-hand side) and GH (Upper right-hand side)

Parameters	AGE	SBP	DBP	GA	WT	BMI	TC	HDL	TG	LDL	VLDL	AI	MDA
AGE		0.10	0.11	-0.03	0.14	0.12	0.03	-0.22	0.05	0.04	0.05	0.20	0.24
SBP	-0.05		0.52***	0.13	0.09	0.11	0.00	-0.18	-0.05	0.05	-0.04	0.17	0.49**
DBP	-0.26	0.30		0.29*	0.05	0.10	0.07	0.05	-0.17	0.07	-0.18	0.12	0.11
GA	-0.16	-0.19	-0.02		0.11	0.10	-0.12	-0.01	0.18	-0.11	0.18	0.04	0.67**
WT	0.45**	-0.40**	-0.28	-0.15		0.94***	-0.03	0.00	-0.04	-0.03	-0.04	-0.02	-0.05
BMI	0.44**	-0.40**	-0.31	0.11	0.83***		0.06	-0.05	0.03	0.06	0.03	0.09	0.00
TC	-0.12	0.26	-0.20	-0.03	-0.25	-0.39*		-0.17	-0.13	0.94***	-0.13	0.47	0.27
HDL	0.11	0.16	-0.55***	0.22	-0.11	-0.06	0.66***		-0.27	-0.41**	-0.27	-0.85***	0.23
TG	0.04	0.24	-0.30	-0.06	-0.17	-0.33	0.94***	0.73***		-0.21	0.99***	0.29*	0.22
LDL	-0.45**	0.12	0.34	-0.02	-0.27	-0.33	0.40**	-0.16	0.09		-0.21	0.62***	-0.07
VLDL	0.11	0.16	-0.55***	0.22	-0.11	-0.06	0.66***	0.99***	0.73***	-0.16		0.29*	0.35*
AI	0.40**	0.05	-0.53***	-0.05	0.05	-0.01	0.34	0.63***	0.61***	-0.67***	0.63***		0.33*
MDA	0.65***	0.09	-0.16	0.02	0.13	0.08	0.63***	0.25	0.68***	-0.05	0.31*	0.56***	

*Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed), ***Correlation is significant at the 0.001 level (2-tailed). SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, BMI: Body Mass Index, TC: Total serum cholesterol, GA: Gestation age, WT: Weight, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, VLDL: Very Low Density Lipoprotein, AI: Atherogenic Index, MDA: Malondialdehyde

Generally, there is no significant correlation between the clinical variables and lipid profile in relation to MDA within the control group. However, there is a significant positive correlation between blood pressure (SBP and DBP) and MDA among the PIH group (Table 3). Apart from VLDL and AI which gave significant positive correlation with MDA among both PE and GH, age, TC and TG also correlate positively with MDA among PE subjects. SBP and GA are additional factors that correlate significantly with MDA among the GH group (Table 4).

Apart from HDL which gave a negative but significant correlation with AI within the control group, TC, LDL and TG correlate positively with AI. With the exception of LDL which indicates a negative but significant correlation, TC, HDL and TG indicated significant positive correlation with AI among the PIH subjects (Table 3). Similar to PIH, subjects within the PE subgroup gave significant negative correlation between LDL and DBP in relation to AI and a significant positive correlation with age, HDL, TG and VLDL. Also, in both the control group (CG) and GH group, AI showed significant positive correlation with TG, LDL and VLDL and negative significant correlation with HDL (Table 4).

LDL gave a significant negative correlation with HDL among all the studied groups except for PE where the negative correlation did not reach a significant level (Table 3, 4). Among the PIH group, TC showed a significant positive correlation with HDL, TG and LDL (Table 3); where as among the PE group, there was a positive correlation between TC and HDL, TG, LDL as well as VLDL (Table 4).

DISCUSSION

The literature suggests that PIH (PE and GH) is a widespread inflammatory state where a number of plasma factors that regulate endothelial functions are altered (Gratacos, 2000; Williams and de Swiet, 1997). An endothelial hyperstimulation is initially provoked, eventually leading to severe endothelial dysfunction and resulting in distributed microangiopathic disease with vasospasm and hypercoagulation (Cekmen *et al.*, 2003; Gratacos, 2000).

Increased BMI examined in the present study could partly explain the significant increase in TG and LDL because increase in weight and BMI is associated with

increase in body fat percentage levels. It is known that PIH (PE and GH) is associated with hypertriglyceridemia (Williams and de Swiet, 1997). This study also confirmed the increases in the level of triglyceride among these groups as compared to the control. The principal modulator of this hypertriglyceridemia is oestrogen as pregnancy is associated with hyperoestrogenaemia. Oestrogen induces hepatic biosynthesis of endogenous triglycerides, by increasing the hepatic VLDL-TG synthesis and secretion and plasma TG concentration (Glueck *et al*., 1975). This process may be modulated by hyperinsulinism found in pregnancy (Adegoke *et al*., 2003). The above mentioned interactions along with increased endothelial triglyceride accumulation may result in endothelial cell dysfunction during gestation (Mikhail *et al*., 1995). Increased TG, found in pregnancy induced hypertension, is likely to be deposited in predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense LDL (Sattar *et al*., 1997a). Moreover, this hypertriglyceridemia may be associated with hypercoagulability (Kokia *et al*., 1990).

Additionally, in this study, significantly high levels of LDL-C concentration were found in Ghanaian women presenting with PIH, PE and GH. However, total cholesterol and AI levels in these groups did not reach significant levels. These results are consistent with the findings reported in studies of other populations (Cekmen *et al*., 2003). A significant fall in LDL-C concentration in the control group as observed in this present study may be attributed to hyperoestrogenaemia, while LDL-C levels increased significantly in the PIH subjects (Hubel *et al*., 1998; Sattar *et al*., 1997b). Moreover, other studies have also demonstrated that there is a predominance of the atherogenic small low-density lipoproteins (LDL) and that vascular cell adhesion molecules are increased in association with hyperlipidemia in PIH (PE and PE) (Hubel *et al*., 1998; Sattar *et al*., 1997a). Though the relevance of the lipid profile ratios (LDL-C/HDL-C; TC/HDL-C; TG/HDL-C and HDL-C/VLDL-C) in pregnancy and PIH is yet to be established, the significance of altered TG/HDL-C ratios cannot be overlooked as it may indicate additional risks in PIH.

The endothelial dysfunction in PIH could originate from oxidative stress as well as dyslipidaemia. Free radicals can be generated by many different enzymatic processes. They are extremely reactive and interact with polyunsaturated fatty acids to produce lipid peroxides with a much longer half-life (Gratacos, 2000; Madazli *et al*., 1999; Williams and de Swiet, 1997).

The increase in MDA levels found in this study is in agreement with the results of other studies (Jain and Wise, 1995; Madazli *et al*., 1999) which support the notion that lipid peroxidation is an important factor in the pathogenesis of PIH (PE and GH). Furthermore, serum MDA levels were highest in the PE group than PIH and GH (Fig. 1). These results suggest that the extent of lipid peroxidation probably correlates with the severity of the disorder. The increase in MDA is strongly related to lipid peroxidation caused by oxidative stress and is expected to affect various tissues and organ systems, including vascular endothelium. When oxidative stress reaches a certain level, cellular damage occurs, including structural damage in cellular membranes, in mitochondrial and nuclear DNAs and impairment of enzymatic functions at multiple levels. Oxidative stress can have an effect mainly on endothelial vessels and on many tissues and organs both locally and systematically (Cekmen *et al*., 2003). During these processes, other molecules involved in vasodilatation such as nitric oxide are inhibited by high lipid peroxide concentration (Gratacos, 2000; Williams and de Swiet, 1997). Presumably, all these circumstances may play roles in the ethiopathogenesis of hypertension in PIH.

There have been studies which suggested that endothelial changes in PIH pathophysiology might be related to either an increase or a decrease in the synthesis of nitric oxide (NO). The NO and MDA levels may possibly be related to the pathogenesis of PIH (PE and GH) because, dysfunction of endothelial cells can contribute to inappropriate vasoconstriction and platelet aggregation which are early signs of atherosclerosis, hypertension and coronary vasospasm (Vane and Botting, 1992) Evidence indicates that NO can have either a pro-oxidant or an anti-oxidant effect on lipid peroxidation, depending on a variety of contingent factors (Paternoster *et al*., 1999). At relatively high concentrations, NO can attenuate membrane dysfunction and tissue injury, while acting as a reactive oxygen metabolite (D'Ischia *et al*., 2000).

On the other hand, when generated at lower concentrations in the presence of oxygen, superoxide and other reactive oxygen species, NO can be converted into a range of potent oxidants (such as nitrogen dioxide and peroxynitrite) which might amplify and exacerbate the harmful effects of lipid peroxidation (O'Donnell *et al*., 1997). The reduced release of vasodilating agents such as nitric oxide (NO) may lead to hypertension (Erel *et al*., 1999). NO is a potent vasodilatator and is thought to have a major effect on gestational vasodilatation (Ludwig *et al*., 1997; Narin *et al*., 2000). Altered production of NO by the vascular endothelium may influence the pathogenesis of pre-eclampsia (Ludwig *et al*., 1997; Narin *et al*., 2000). This could probably explain the significant positive correlation between blood pressure and MDA among the PIH group.

CONCLUSION

In conclusion, the findings of this current study suggest that an abnormal lipid metabolism and particularly high triglycerides, LDL-C and lipid peroxides may contribute to the promotion of oxidative stress and vascular dysfunction seen in PIH and preeclampsia. It is, therefore, imperative that, blood lipid concentrations and lipid peroxides be evaluated in pregnant women during antenatal care since it could be helpful in the early detection and prevention of obstetric complications such as PIH.

REFERENCES

Adegoke, O.A., E.E. Iyare and S.O. Gbenebitse, 2003. Fasting plasma glucose and cholesterol levels in pregnant Nigerian women. Niger. Postgraduate Med. J., 10: 32-36.

Bartham, D. and P. Trinder, 1972. An improved colour reagent for the determination of blood glucose by the oxidase system. Analyst, 97: 142-145.

Bellany, L., J.P. Casas, A.D. Hingorani and D.J. Williams, 2007. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: Systematic review and Meta-analysis. Br. Med. J., 335: 974-974.

Belo, L., M. Caslake, D. Gaffney, A. Santos-Silva, L. Pereira-Leite, A. Quintanilha and I. Rebelo, 2002. Changes in LDL size and HDL concentration in normal and preeclamptic pregnancies. Atherosclerosis, 162: 425-432.

Cekmen, M.B., A.B. Erbagci, A. Balat, C. Duman, H. Maral, K. Ergen, M. Ozden, O. Balat and S. Kuskay, 2003. Plasma lipid and lipoprotein concentrations in pregnancy induced hypertension. Clin. Biochem., 36: 575-578.

D'Ischia, M., A. Palumbo and F. Buzzo, 2000. Interactions of nitric oxide with lipid peroxidation products under aerobic conditions: Inhibitory effects on the formation of malondialdehyde and related thiobarbituric acid-reactive substances. Nitric Oxide, 4: 4-14.

Erel, C.T., L.M. Senturk, E. Oral, H. Mutlu, U. Colgar, H. Seyisoglu and E. Ertungealp, 1999. Results of the ACTH stimulation test in hirsute women. J. Reprod. Med., 44: 247-252.

Forest, J.C., J. Girouard, J. Masse, J.M. Moutquin, A. Kharfi, R.B. Ness, J.M. Roberts and Y. Giguere, 2005. Early occurrence of metabolic syndrome after hypertension in pregnancy. Obstet. Gynecol., 105: 1373-1380.

Friedman, S.A., R.N. Taylor and J.M. Roberts, 1991. Pathophysiology of preeclampsia. Clin. Perinatol., 18: 661-682.

Glueck, C.J., R.W. Fallat and D. Scheel, 1975. Effects of estrogenic compounds on triglyceride kinetics. Metabolism, 24: 537-545.

Gratacos, E., 2000. Lipid-mediated endothelial dysfunction: A common factor to preeclampsia and chronic vascular disease. Eur. J. Obstet. Gynecol. Reprod. Biol., 92: 63-66.

Gulmezoglu, A.M., G.J. Hofmeyr and M.M. Oosthuisen, 1997. Antioxidants in the treatment of severe pre-eclampsia: An explanatory randomised controlled trial. Br. J. Obstet. Gynaecol., 104: 689-696.

Hubel, C.A., 1999. Oxidative stress in the pathogenesis of preeclampsia. Proc. Soc. Exp. Biol. Med., 222: 222-235.

Hubel, C.A., F. Lyall, L. Weissfeld, R.E. Gandley and J.M. Roberts, 1998. Small low-density lipoproteins and vascular cell adhesion molecule-1 are increased in association with hyperlipidemia in preeclampsia. Metabolism, 47: 1281-1288.

Hubel, C.A., J.M. Roberts, R.N. Taylor, T.J. Musci, G.M. Rogers and M.K. McLaughlin, 1989. Lipid peroxidation in pregnancy: New perspectives on preeclampsia. Am. J. Obstet. Gynecol., 161: 1025-1034.

Jain, S.K. and R. Wise, 1995. Relationship between elevated lipid peroxides, vitamin E deficiency and hypertension in preeclampsia. Mol. Cell. Biochem., 151: 33-38.

Kaaja, R., M.J. Tikkanen, L. Viinikka and O. Ylikorkala, 1995. Serum lipoproteins, insulin and urinary prostanoid metabolites in normal and hypertensive pregnant women. Obstet. Gynecol., 85: 353-356.

Kamal, A.A., A. Gomaa, M. el Khafif and A.S. Hammad, 1989. Plasma lipid peroxides among workers exposed to silica or asbestos dusts. Environ. Res., 49: 173-180.

Kirkendall, W.M., A.C. Burton, F.H. Epstein and E.D. Freis, 1967. Recommendations for human blood pressure determination by sphygmomanometers. Circulation, 36: 980-988.

Kokia, E., G. Barkai, B. Reichman, P. Segal, B. Goldman and S. Mashiach, 1990. Maternal serum lipid profile in pregnancies complicated by hypertensive disorders. J. Perinat. Med., 18: 473-478.

Krishna Mohan, S. and G. Venkataramana, 2007. Status of lipid peroxidation, glutathione, ascorbic acid, vitamin E and antioxidant enzymes in patients with pregnancy-induced hypertension. Indian J. Physiol. Pharmacol., 51: 284-288.

Ludwig, M., M. Morris and C.D. Sladek, 1997. Effects of antisense oligodeoxynucleotides on peptide release from hypothalamoneurohypophysial explants. Am. J. Physiol. Regulat. Integrat. Comparat. Physiol., 41: R1441-R1446.

Madazli, R., A. Benian, K. Gumustas, H. Uzun, V. Ocak and F. Aksu, 1999. Lipid peroxidation and antioxidants in preeclampsia. Eur. J. Obstet. Gynecol. Reprod. Biol., 85: 205-208.

Meyer, N.L., B.M. Mercer, S.A. Friedman and B.M. Sibai, 1994. Urinary dipstick protein: A poor predictor of absent or severe proteinuria. Am. J. Obstet. Gynecol., 170: 137-141.

Mikhail, M.S., J. Basu, P.R. Palan, J. Furgiuele, S.L. Romney and A. Anyaegbunam, 1995. Lipid profile in women with preeclampsia: Relationship between plasma triglyceride levels and severity of preeclampsia. J. Assoc. Acad. Minor. Phys., 6: 43-45.

Mutlu-Turkoglu, U., E. Ademoglu, L. Ibrahimoglu, G. Aykac-Toker and M. Uysal, 1998. Imbalance between lipid peroxidation and antioxidant status in preeclampsia. Gynecol. Obstet. Invest., 46: 37-40.

Narin, F., N. Narin, H. Pasaoglu, K. Uzum and R. Erdogan, 2000. Nitric oxide level in children with pulmonary hypertension. Indian J. Physiol. Pharmacol., 44: 335-339.

O'Donnell, V.B., P.H. Chumley, N. Hogg, A. Bloodsworth, V.M. Darley-Usmar and B.A. Freeman, 1997. Nitric oxide inhibition of lipid peroxidation: Kinetics of reaction with lipid peroxyl radicals and comparison with alpha-tocopherol. Biochemistry, 36: 15216-15223.

Osei-Nketiah, S., 2001. Maternal mortality at Effia nkwanta Regional Hospital, Ghana-A one year review (January-December, 1998). Ghana Med. J., 35: 124-129.

Ozan, H., Y. Ilcol, Y. Kimya, C. Cengiz and B. Ediz, 2002. Plasma anti-oxidant status and lipid profile in non-gravida women with a history of pre-eclampsia. J. Obstet. Gynaecol. Res., 28: 274-279.

Paternoster, D.M., A. Stella, M. Mussap, M. Plebani, G. Gambaro and P.V. Grella, 1999. Predictive markers of pre-eclampsia in hypertensive disorders of pregnancy. Int. J. Gynaecol. Obstet., 66: 237-243.

Plaa, G.L. and H. Witschi, 1976. Chemicals, drugs and lipid peroxidation. Annu. Rev. Pharmacol. Toxicol., 16: 125-141.

Roberts, J.M., 1998. Endothelial dysfunction in preeclampsia. Semin Reprod. Endocrinol., 16: 5-15.

Roberts, J.M., R.N. Taylor, T.J. Musci G.M. Rodgers, C.A. Hubel and M.K. McLaughlin, 1989. Preeclampsia: An endothelial cell disorder. Am. J. Obstet. Gynecol., 161: 1200-1204.

Sato, M., T. Miyazaki, T. Nagaya, Y. Murata, N. Ida, K. Maeda and H. Seo, 1996. Antioxidants inhibit tumor necrosis factor-alpha mediated stimulation of interleukin-8, monocyte chemoattractant protein-1 and collagenase expression in cultured human synovial cells. J. Rheumatol., 23: 432-438.

Sattar, N., A. Bendomir, C. Berry, J. Shepherd, I.A. Greer and C.J. Packard, 1997. Lipoprotein subfraction concentrations in preeclampsia: Pathogenic parallels to atherosclerosis. Obstet. Gynecol., 89: 403-408.

Sattar, N., I.A. Greer, J. Louden, G. Lindsay, M. McConnell, J. Shepherd and C.J. Packard, 1997. Lipoprotein subfraction changes in normal pregnancy: Threshold effect of plasma triglyceride on appearance of small, dense low density lipoprotein. J. Clin. Endocrinol. Metab., 82: 2483-2491.

Schonfeld, G., 1979. Lipoproteins in atherogenesis. Artery, 5: 305-329.

Seely, E.W. and C.G. Solomon, 2003. Insulin resistance and its potential role in pregnancy-induced hypertension. J. Clin. Endocrinol. Metab., 88: 2393-2398.

Shlafer, M. and B.M. Shepard, 1984. A method to reduce interference by sucrose in the detection of thiobarbituric acid-reactive substances. Anal. Biochem., 137: 269-276.

Sies, H., 1991. Oxidative stress: From basic research to clinical application. Am. J. Med., 91: 31S-38S.

Solomon, C.G. and E.W. Seely, 2001. Brief review: Hypertension in pregnancy: A manifestation of the insulin resistance syndrome? Hypertension, 37: 232-239.

Trinder, P., 1969. Determination of blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen. J. Clin. Pathol., 22: 158-161.

Turpin, C.A., L. Ahenkorah, W.K.B.A. Owiredu, E.F. Laing and N. Amidu, 2008. The prevalence of the metabolic syndrome among Ghanaian Pregnancy-Induced Hypertensive patients using the World Health Organisation and the National Cholesterol Education program III criteria. J. Med. Sci., 8: 443-451.

Vane, J.R. and R.M. Botting, 1992. The role of chemical mediators released by the endothelium in the control of the cardiovascular system. Int. J. Tissue React., 14: 55-64.

Williams, D.J. and M. de Swiet, 1997. The pathophysiology of pre-eclampsia. Intensive Care Med., 23: 620-629.