Annals of Medical Laboratory Science (2021) **1**(2): 39 - 49
https://www.annalsmls.org
https://doi.org/10.51374/annalsmls.2021.1.2.0041

Placental Oxidative Stress in the pathogenesis of Hypertensive Disorders of Pregnancy

Martin Awe Akilla[1]*, Peter Paul Mwinsanga Dapare[2], Eric Misho Bawa[2], Benedict Boateng Antuamwine[2], Ignatius Abowini Nchor Awinibuno[2]

[1]Department of Medical Laboratory Technology, Bolgatanga Technical University, Bolgatanga; [2]Department of Biomedical Laboratory Science, School of Allied Health Sciences, University for Development Studies, Tamale, Ghana.
**Corresponding Author: E-mail: akillamgh78@gmail.com*

How to cite this paper: Akilla, M.A., Dapare, P.P.M., Bawa, E.M., Antuamwine, B.B., and Awinibuno, I.A.N. (2021) Placental Oxidative Stress in the pathogenesis of Hypertensive Disorders of Pregnancy. *Annals of Medical Laboratory Science 1(2): 39 - 49*

Received: December 19, 2020
Accepted: March 10, 2021
Published: June 20, 2021

ABSTRACT

Background: Hypertensive disorders of pregnancy are a major complication of pregnancies and can lead to fetal growth retardation, premature delivery and maternal morbidity and mortality. The study aimed at assessing the potential role of the placenta in the pathogenesis of hypertensive disorders of pregnancy.

Methods: This study was a case-control study conducted at the Upper East Regional Hospital, Ghana from September, 2016 to March 2017.Twenty (20) pregnant women with hypertensive disorders of pregnancy (i.e., Pregnancy induced hypertension, preeclampsia and eclampsia) as cases and 30 normotensive pregnancies as controls, were included in the study. The placenta was excised after delivery, homogenized and assayed for malondialdehyde, catalase, total peroxide, oxidative stress index, total antioxidant capacity and placental lipid profile.

Results: The ages of the two groups were similar, with malondialdehyde ($p = 0.001$) and Oxidative Stress Index ($p < 0.001$) being significantly higher in the hypertensive group compared to the control group whereas Total Antioxidant Capacity ($p < 0.001$) and Catalase ($p = 0.011$) were significantly higher in the control group compared to the hypertensive group. The proportion of normal, term and livebirth deliveries were significantly higher among controls compared to the hypertensive disorders of pregnancy group. Among the estimated oxidative stress markers, total antioxidant capacity turned out to be the best predictor of the hypertensive disorders of pregnancy.

Conclusion: Our findings suggest oxidative stress in women with hypertensive disorders of pregnancy and that placental oxidative stress could be the driving factor for the pathogenesis and severity of these hypertensive disorders of pregnancy.

Annals of Medical Laboratory Science (2021) 1(2), 39 - 49

Keywords: Oxidative stress, eclampsia, pregnancy induced hypertension

INTRODUCTION

Hypertensive disorders of pregnancy may be described as hypertension with the presence or absence of proteinuria and edema, with the clinical presentation usually occurring late in pregnancy and resolving after delivery (Sravanthi *et al.*, 2017). These usually include pregnancy induced hypertension (PIH), pre-eclampsia and eclampsia, with a general incidence of five to ten per cent of all pregnancies (Mohanty *et al.*, 2006), hypertensive disorders in pregnancy are a major complication of pregnancies and can lead to fetal growth retardation, premature delivery and maternal morbidity and mortality (Saczko *et al.*, 2002b). Pregnancy related morbidity and mortality relies on the severity of the hypertension and there is no known way of preventing its complications (Sravanthi *et al.*, 2017). The impact of these disorders on maternal and foetal outcomes can therefore not be underestimated.

The pathogenesis of this disorder remains a

https://doi.org/10.51374/annalsmls.2021.1.2.0041

controversy (Hubel, 1999) even though endothelial dysfunction has been largely implicated in its pathogenesis. In endothelial dysfunction, there is an altered state of endothelial cell differentiation in response to sub-lethal injury or cytotoxic stimulation. Maternal hypertension and reduced blood flow to organs occur as a result of increased generalized vasoconstriction (Das *et al.*, 2012). Other factors that have been implicated in the pathogenesis of PIH include immunological intolerance between maternal and feto-placental tissue, cardiovascular maladaptation and vasoconstriction, platelet activation and genetic disposition (Kintiraki *et al.*, 2015). Oxidative stress has also been given considerable attention in its relationship with pregnancy and its complications (Sheena, 2012).

Oxidative stress plays a major role in the pathogenesis and development of many diseases (Dandana *et al.*, 2011). It is an imbalance between reactive oxygen species (ROS) and the antioxidant mechanism leading to excessive production of oxygen metabolites in a cell (Oghagbon *et al.*, 2016). ROS are highly reactive metabolites, free radicals derived from molecular oxygen and nitrogen (Sheena, 2012). Oxidative stress results in endothelial injury and dysfunction by increased production of lipid peroxides and free radicals (Saxena *et al.*, 2016). Oxidative stress can initiate a number of damaging reactions, including oxidative destruction of macromolecules such as lipids, proteins and nucleic acids in the placenta, brain, liver and kidneys (Sheena, 2012). The deleterious effects of ROS on cells are minimized by the production of naturally occurring antioxidants (Sheena, 2012).

Studies have reported high levels of oxidative stress in the human placenta, suggesting that it could be as a result of high placental polyunsaturated fatty acids which are highly predisposed to the attack by ROS (Mehendale *et al.*, 2008; Negre-Salvayre *et al.*, 2010) without quantifying the levels of placental lipids associated with these oxidative stress levels in both normal and abnormal pregnancies. Furthermore, these assertions are not clear, as to whether the resultant PIHs were due to localised oxidative stress in the maternal adipose tissue (Pou *et al.*, 2007) or the placental tissue (Myatt and Cui, 2004). The involvement of the human placental lipids in fuelling oxidative stress leading to the development of PIH is hypothetical especially among a population of African pregnant women. This study is therefore aimed at investigating the levels of placental lipids and oxidative stress in normal and PIH pregnancies at delivery in the Upper East Regional Hospital (Bolgatanga Ghana).

MATERIALS AND METHODS

Study Design

This study was a case – control study which was carried out at the maternity ward of the Upper East Regional Hospital (Bolgatanga-Ghana).

ETHICAL APPROVAL

The study was approved by the Navrongo Health Research Centre Institutional Review Board. Verbal informed consent was obtained from all pregnant women who agreed to participate. Pregnant women were assured that refusal to participate will not affect care being given to them at the hospital.

Subjects

A purposive sampling method was used in recruiting study subjects. Fifty (50) pregnant women who consented prior to delivery, were administered with a short questionnaire to obtain clinical and obstetric information. The gestational age at birth was estimated based on date of last menstrual period as well as ultrasonography report. Infants born between 28 and 37 weeks were considered preterm. Singletons weighing less than 2,500 grams were considered as low birth weight babies (LBW).

Pre-eclampsia was defined as pregnancy in women who were diagnosed with sustained systolic blood pressure above 140mmHg, diastolic blood pressure above 90mmHg and sustained proteinuria with 300 mg protein/24 hr urinary sample in the absence of urinary tract infection. The blood pressure readings were documented on at least two occasions at four hours apart.

Placentae were collected from thirty (30) mothers

https://doi.org/10.51374/annalsmls.2021.1.2.0041

without any adverse conditions in pregnancy (controls), twelve (12) pre-eclamptic pregnant women and eight (8) eclamptic pregnant women, making a total of twenty (20) cases. The placentae were observed for their colours and the insertion of cord after which the weight of the babies and placentae were determined using a weighing scale (Seca).

Data Collection

Anthropometric parameter measurements

Body weight was measured (to the nearest 0.5 kilogram) with the subject standing on an electrical weighing scale (Seca Alpha, GmbH&CO., Igni, France; range 0.1-150 kg, precision 100g) wearing light clothing. The weighing scale was calibrated using known weights from Ghana standard authority. Height was measured (to the nearest 1.0 millimeter) with the Subject standing in an erect position against a vertical scale of portable stadiometer (Pfifter, Carlstadt, N.J,U.S.A ; range 70-205cm, precision 1mm), with their heads positioned so that the top of the external auditory meatus was in level with the inferior margin of the bony orbit. All measurements were made in duplicates, to the nearest centimeter and the mean values were used for subsequent analysis. BMI was calculated as weight in kilograms divided by squared of the height in meter.

Blood Pressure measurements

Blood pressures were measured two times in a seated position after 15 min of rest using a standard mercury sphygmomanometer (by observing the appearance of the first and the disappearance of the fifth Korotkoff sound); measurements were made between the hours of 7:00am and 10:00 am. High systolic blood pressure (SBP) and high diastolic blood pressure (DBP) were defined using WHO, 1998 criteria.

Biochemical Data

Placental Tissue processing

About 25 to 60g (about 1-2 cotyledons) of placental tissue was cut from the villous tree of each placenta within one hour after delivery and extensively rinsed with phosphate buffered saline (PBS) to remove excess blood and stored frozen at -80°C or homogenized in about 0.5g tissue per 1 ml of ice-cold phosphate buffered saline (KCl 140 mmol/ L, phosphate (20 mmol/L, pH 7.4) (PBS). The homogenates were centrifuged for 15 minutes at 5000 x g at -20°C after which the supernatant was removed and assayed immediately or aliquoted and stored at -80°C.

Blood: About 4.0 ml of venous blood samples from overnight fasting subjects was aseptically collected the serum separated and stored at -20°C until ready for biochemical analysis. The blood and supernatants from the placental homogenates were analysed for triglyceride, total cholesterol, and HDL -cholesterol, using Envoy® 500 reagents (Vital Diagnostics, USA) according to the manufacture's specification on BT 5000® Random Access Chemistry Analyser (Biotecnica, Italy).

Placental MDA

The determination of oxidative stress levels was analysed by adopting the method described by Kamal *et al*., (1989) and Shlafer and Shepard (1984). The thiobarbituric acid (TBA) reacting substances (TBARS) assay was used as an indicator of lipid peroxidation and levels of free radicals in the placenta samples. The assay is based on the reaction of TBA with Malondialdehyde (MDA); one of the aldehyde products of lipid peroxidation at the optimum pH and temperature conditions and the amount of MDA–TBA adduct produced was then measured. To increase the sensitivity, the complex was extracted into an organic solvent (n-butanol). The absorbance of the supernatant was measured at 535nm wavelength on spectrophotometer (HUMALYZER JUNIOR) and the results expressed in umol/L using the extinction coefficient of 1.56 X105 Lmmol-1cm (Buege and Aust, 1978).

Total Antioxidant Capacity (TAC) TEST

Total antioxidant status was measured using Koracevic *et al.* (2001) method. It is based on the principle that a standardised solution of Fe-EDTA complex reacts with hydrogen peroxide (Fenton reaction) to give hydroxyl radical, a reactive oxygen species. This reactive oxygen species degrades

https://doi.org/10.51374/annalsmls.2021.1.2.0041

benzoate to produce thiobarbiturate reacting substances (TBARS). The antioxidant from added sample causes suppression of the production of TBARS. Therefore, the decrease in the concentration of TBARS as a result of antioxidants is measured spectrophotometrically and serves as concentration of antioxidants present in the placental sample added.

Total Peroxide Concentration (TP)

Total Peroxide (TP) concentrations was determined using the FOX2 method (Miyazawa, 1989) with minor modifications (Harma *et al.*, 2005; Yeni *et al.*, 2005). The FOX2 test system is based on oxidation of ferrous ion to ferric ion by various types of peroxides contained within the placenta samples, to produce a coloured ferric-xylenol orange complex whose absorbency can be measured at 560nm.

Oxidative Stress Index (OSI)

The percentage ratio of the TP to the TAC gives the Oxidative Stress Index (OSI), an indicator of the degree of oxidative stress (Yanik *et al.*, 2004; Harma *et al.*, 2005; Yeni *et al.*, 2005). To perform the calculation, the result unit of TAC, mmol Trolox equivalent L^{-1}, was converted to µmol equivalent L^{-1} and the OSI value was calculated by the formula:

OSI = [(TP, µmol L^{-1})/(TAC, µmol Trolox equivalent L^{-1}) x 100]

Lipid Profile

Triglyceride, total cholesterol, HDL-cholesterol were assayed using Envoy® 500 reagents (Vital Diagnostics, USA) according to the manufacture's specification on BT 5000® Random Access Chemistry Analyzer (Biotecnica, Italy). LDL-cholesterol was calculated based on Friedwald's equation as follows;
LDL-chol = total chol-(triglycerides/2.2 + HDL) mmol/L.

Statistical Analysis

Data was analysed using Microsoft Excel 2016 and GraphPad Prism version 6.01 (Graph Pad Software, San Diego California USA, www.graphpad.com). Various statistical tests were employed in the analysis and in all cases, a p values < 0.05 was considered statistically significant.

RESULTS

Twenty (20) cases of pregnancy induced hypertension (PIH) and 30 normotensive pregnant women (controls), were recruited for this study. The ages of the PIH group and those of the control group were similar (PIH; 29.4±6.6 vs control; 26.8 ± 6.4, p=0.17). Gestational age at delivery was

Table 1: Anthropometry, gestational history and placental lipid profile of the study population

Parameters	Cases (n = 20)	Controls (n = 30)	P Value
Age	29.4 ± 6.6	26.8 ± 6.4	0.17
Parity	2.1 ± 1.8	1.3 ± 1.1	0.09
Gravidity	3.1 ± 1.8	2.3 ± 1.4	0.11
Gestational Age	36.4 ± 6.2	39.0 ± 1.6	0.04
Body Mass Index	28.6 ± 6.7	25.0 ± 4.5	0.03
Systolic Blood Pressure	159.6 ± 18.4	111.7 ± 10.4	< 0.001
Diastolic Blood Pressure	101.4 ± 11.8	68.1 ± 9.0	< 0.001
Placental cholesterol (mg/dl)	34.8 ± 10.1	36.0 ± 8.3	0.66
Placental HDL-C (mg/dl)	2.0 ± 0.9	2.0 ± 0.8	0.95
Placental LDL-C(g/dl)	6.1 ± 3.8	6.7 ± 5.2	0.67
Placental LDL/HDL	3.7 ± 3.3	3.3 ± 3.1	0.69
Placental TC/HDL	18.3 ± 7.4	17.3 ± 8.8	0.68
Placental TG/HDL	84.8 ± 37.2	79.7 ± 44.7	0.68
Placental HDL/VLDL	0.1 ± 0.0	0.1 ± 0.0	0.76
Placental VLDL-C(mg/dl)	24.4 ± 7.9	25.4 ± 6.1	0.61
Placental triglyceride (mg/dl)	159.8 ± 52.1	165.1 ± 39.7	0.68

Data presented as mean ± standard deviation; p-value <0.05 considered statistically significant

https://doi.org/10.51374/annalsmls.2021.1.2.0041

significantly higher (p=0.04) in controls than in cases whiles BMI at early pregnancy (p=0.03), systolic blood pressure (p<0.001), diastolic blood pressure (p<0.001) were significantly higher in the PIH group compared to the control group (Table 1).

The mean malondialdehyde (MDA), total antioxidant capacity (TAC), catalase, total peroxide and Oxidative Stress Index for the PIH group was 15.2 ± 5.4 mmol/ml, 6.5 ± 2.3 mmol/l, 4.7 ± 3.3 U/g, 23.0 ± 7.1 (mmol/l), 4.3 ± 2.5 respectively for the PIH group and 10.4 ± 4.54 mmol/ml, 14.1 ± 1.8 mmol/l, 7.0 ± 2.8 U/g, 22.0 ± 9.6 mmol/l and 1.6 ± 0.7 respectively for the control group. Malondialdehyde (p=0.001) and oxidative stress index (p < 0.001) was significantly higher in the PIH group compared to the control group whereas total antioxidant capacity (p < 0.001) and Catalase (p=0.01) were significantly higher in the control group compared to the PIH group (Table 2).

Among the PIH subjects, a comparison in the levels of oxidative stress indices was made between those who were diagnosed with preeclampsia and those diagnosed with gestational hypertension. There were no significant variations in the levels of oxidative stress markers as shown in Table 3.

Table 2. Comparison of Placental Oxidative Stress Markers in cases and controls

Parameters	Cases (n = 20)	Controls (n = 30)	P value
Malondialdehyde (nmol/ml)	15.2 ± 5.4	10.4 ± 4.5	0.001
Total Antioxidant Capacity (mmol/L)	6.5 ± 2.3	14.1 ± 1.8	< 0.001
Catalase (U/g)	4.7 ± 3.3	7.0 ± 2.8	0.01
Total Peroxide (mmol/L)	23.0 ± 7.1	22.0 ± 9.6	0.71
Oxidative Stress Index	4.3 ± 2.5	1.6 ± 0.7	< 0.001

Table 3. The comparison of the levels of oxidative stress markers between preeclamptic and gestational hypertensive subjects.

Parameters	Pre-eclampsia (PE)	Gestational Hypertension	P-value
MDA (nmol/ml)	14.63±4.30	17.20±1.35	0.83
TAC (mmol/L)	6.44±2.37	6.50±2.38	0.96
Catalase (U/g)	6.04±2.60	6.25±2.17	0.90
Total Peroxide (mmol/L)	25.36±6.36	20.81±3.24	0.19
OSI	4.88±2.41	3.78±2.17	0.42

PE; preeclampsia, GH; gestational hypertension, MDA; malondialdehyde, TAC; total antioxidant capacity, OSI; oxidative stress index. Values are mean ± SD. Comparisons between the two groups was done using unpaired student t-test

Table 4. Comparison of Pregnancy and delivery outcomes between cases and controls

Parameters	Case (n=20)	Control (n=30)	P-Value
Delivery Mode			
Vaginal Delivery	7/20 (35.0%)	29/30 (96.7%)	< 0.001
Caesarian Section	13/20 (65.0%)	1/30 (3.3%)	
Delivery Complication			
Term	13/20 (65.0%)	30/30 (100.0%)	< 0.001
Preterm	7/20 (35.0%)	0/30 (0.0%)	
Fetal Outcome			
Live Birth	17/20 (85.0%)	30/30 (100.0%)	0.03
Still Birth	3/20 (15.0%)	0/30 (0.0%)	
Babies Weight (g)	2875.0 ± 873.5	3093.0 ± 557.7	0.29
Placenta Length (cm)	20.2 ± 5.9	20.0 ± 3.4	0.92
Placenta Weight (g)	582.5 ± 196.9	633.3 ± 151.1	0.31
Fetal Weight/Plac. Weight	5.2 ± 1.5	5.1 ± 1.2	0.89

https://doi.org/10.51374/annalsmls.2021.1.2.0041

Table 4 shows a summary of pregnancy and baby outcomes. As indicated, the proportion of women in the control group (96.7%, p<0.001) who had a normal vaginal delivery were significantly higher than the proportion of normal deliveries among the cases (35.0%). Similarly, whiles all (100%) deliveries in the control group were carried to term, 65% of the pregnancies among the cases were carried to term (p<0.001). Also, there were significantly more (cases-15% vs control-0.0%, p=0.03) still births recorded among the cases as compared to the controls. Babies' and placental weights at birth were higher among controls than cases but these were not statistically significant.

Malondialdehyde (p<0.01) and oxidative stress index (p<0.01) were significantly higher in subjects who had caesarian delivery as compared to subjects who had normal vaginal delivery, whereas total antioxidant capacity (p<0.001) and catalase (p<0.05) were significantly higher in subjects who had normal vaginal delivery as compared to those who had caesarian delivery. Similarly, malondialdehyde (p<0.05) and oxidative stress index (p<0.05) were significantly higher in subjects who had preterm deliveries as compared to those who carried their pregnancies to term, whiles total antioxidant capacity (p<0.001) was significantly higher in pregnancies carried to term as compared to those with preterm pregnancies. Also, total antioxidant capacity (p< 0.05) and catalase (p<0.05) were significantly higher in live births than in still births as shown in Table 5.

Table 6 shows a correlation of oxidative stress markers and other variables considered in the PIH

Table 5. Placental Oxidative stress markers stratified by delivery mode, delivery complication and foetal outcome

Parameters	Delivery Mode		Delivery Complication		Foetal Outcome	
	Normal	C/S	Term	Preterm	Live Birth	Still Birth
Malondialdehyde	10.8 ± 4.9	16.1 ± 4.7**	11.7 ± 5.3	16.1 ± 4.2*	12.2 ± 5.4	14.2 ± 5.6
Total Antioxidant Capacity	12.8 ± 3.5	6.6 ± 2.7***	11.9 ± 4.0	5.6 ± 2.1***	11.4 ± 4.1	5.3 ± 2.1*
Catalase (U/g)	6.7 ± 2.9	4.3 ± 3.1*	6.3 ± 3.2	4.8 ± 2.6	6.3 ± 3.1	2.5 ± 1.3*
Total Peroxide (mmol/L)	22.3 ± 9.3	22.6 ± 6.9	22.3 ± 9.1	23.1 ± 5.2	22.4 ± 8.9	22.5 ± 5.0
Oxidative Stress Index	2.1 ± 1.7	4.2 ± 2.3**	2.4 ± 2.0	4.4 ± 1.7*	2.5± 2.1	4.5 ± 1.3

Table 6. Association between placental oxidative stress markers and clinical and laboratory variables in the PIH group

Parameters	MDA	TAC	CATALASE	T. PEROXIDE	OSI
Age	-0.09	0.28	-0.23	-0.29	-0.43
Parity	0.07	0.27	-0.33	-0.27	-0.45*
Gravidity	0.06	0.23	-0.40	-0.18	-0.38
Gestational Age	-0.27	0.01	-0.32	-0.15	0.02
BMI	-0.31	0.19	-0.14	-0.40	-0.33
SBP	-0.35	-0.26	-0.37	-0.12	0.17
DBP	-0.06	-0.17	-0.40	-0.01	0.12
P. CHOL	0.47*	0.05	0.36	0.53*	0.14
P. HDL-C	0.13	0.11	0.27	0.30	0.08
P. LDL-C	-0.37	-0.29	-0.40	-0.55*	-0.03
P. VLDL-C	0.19	-0.06	0.17	0.32	0.32
P. TRIG.	0.19	-0.03	0.16	0.33	0.30
Babies Weight (g)	-0.10	0.12	-0.23	-0.18	-0.09
Placenta Length (cm)	-0.15	0.16	-0.18	-0.35	-0.23
Placenta Weight (g)	0.22	0.23	0.02	0.18	-0.07
Fetal Weight/Plac. Weight	-0.36	-0.02	-0.30	-0.40	-0.10

https://doi.org/10.51374/annalsmls.2021.1.2.0041

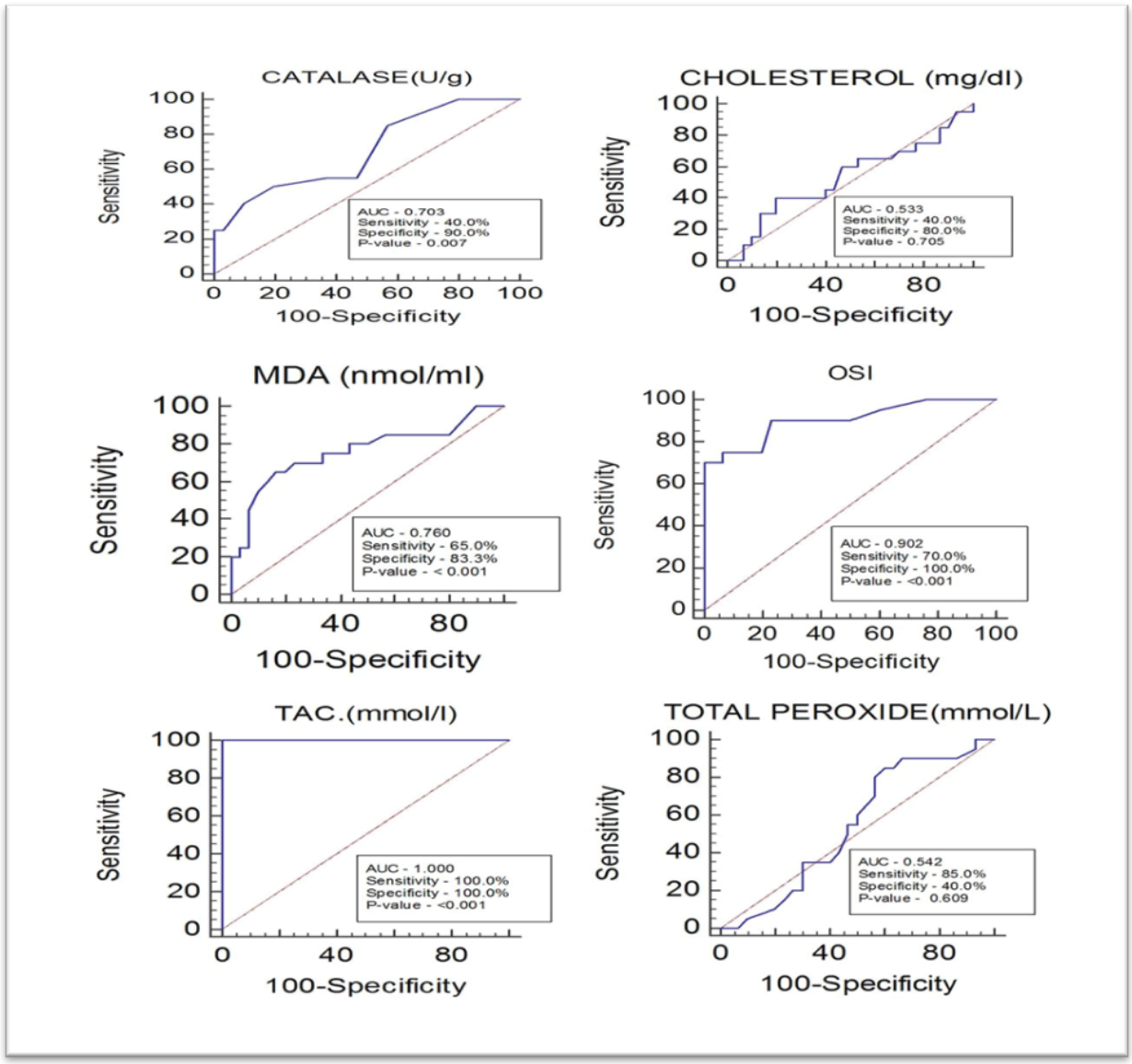

Figure 1. Receive Operator Curves for measured oxidative stress markers in predicting PIH

group. Malondialdehyde and total peroxide were significantly positively associated with total placental cholesterol ($p<0.05$) whiles oxidative stress index and total peroxide were significantly negatively associated with parity ($p<0.05$) and placenta LDL-cholesterol ($p < 0.05$) respectively. With the exception of total placental cholesterol, placental LDL-cholesterol and parity, no significant correlation was detected for the other parameters and measured oxidative stress markers. Catalase and total antioxidant capacity did not show any significant association with any of the variables considered.

DISCUSSION

Oxidative stress is an imbalance in the oxidant-antioxidant concentrations in favour of oxidants, which leads to potential cellular damage (Burton and Jauniaux, 2011). The rise in ROS in circulation is believed to originate from placental generation of ROS during pregnancy (Kurlak *et al.*, 2014). In normal pregnancy, ROS production is

https://doi.org/10.51374/annalsmls.2021.1.2.0041

increased. This increase is essential for proper development of the placenta (Bogavac *et al.*, 2017). Beneficial effects of ROS include cell growth and differentiation (Montuschi *et al.*, 2007) but if unchecked can have detrimental effects. (Sheena, 2012).

The extent of oxidative stress induced by free radicals can be increased by a decreased efficiency in the antioxidant system (Jain *et al.*, 2015). In this study, the role of oxidative stress in the pathogenesis of pregnancy induced hypertension was evaluated.

Placental malondialdehyde (MDA), a product of lipid peroxidation was significantly increased in pregnancy induced hypertension (PIH), indicative of an increased ROS activity in PIH. The findings of this study are consistent with that of Zahoorunnisa *et al.* (2014). In a study of serum lipid profile, malondialdehyde and paraoxonase in normal pregnant women and in pregnant women with preeclampsia, they reported raised levels of malondialdehyde in women with preeclampsia, a complication of hypertension in pregnancy. Zahoorunnisa *et al.* (2014) attributed the increased levels of MDA in PIH to the presence of oxidative stress in PIH. Oxidative injury may occur in placental and maternal compartments because of oxidative stress resulting from increased production of products of lipid peroxidation (Zahoorunnisa *et al.*, 2014). Significantly high MDA concentration in the PIH group is an indication of increased tissue peroxidation in the placentae, resulting in oxidative stress. Therefore, increased MDA concentrations in the PIH group suggest that lipid peroxidation in the placenta plays a role in the pathogenesis of pregnancy induced hypertension.

Catalase, a marker of antioxidant enzyme activity was significantly decreased in the placenta of the PIH group compared to the control group. Similar findings were made by Saczko *et al.* (2002a) in a study on catalase activity in placentas of PIH pregnancies, a decreased catalase activity was reported. Antioxidants scavenge and reduce the presence of free radicals, hence block the effects of free radical damage on cell membranes, cholesterol and nerves (Sheena, 2012). The decrease in placental catalase activity in the PIH group could be due to increased utilization (Zahoorunnisa *et al.*, 2014) or the result of the disturbances in oxidative balance induced by oxidative stress in the placentas of the PIH group. Increased utilization of antioxidants is associated with preeclampsia, a condition in which there is pregnancy induced hypertension (Zahoorunnisa *et al.*, 2014).

In a study carried out by Saczko *et al.* (2002b) to assess the activity of superoxide dismutase in placentas complicated with PIH, it was found out that superoxide dismutase activity was clearly decreased in the PIH group. It is therefore clear that there is a reduction in the antioxidant system in PIH. Reduction in catalase and other enzymes of antioxidant activity as shown in other studies suggest that there could be an increased turn-over of these enzymes to match up arising oxidative burden in PIH.

Total Antioxidant capacity is a measure of the joint action of all antioxidants. The overall defense activity of the system cannot be reflected by any single antioxidant (Bogavac *et al.*, 2017). In this study, total antioxidant capacity was significantly decreased in the PIH group compared to the control. The decrease in total antioxidant capacity in the PIH might be because of inadequate production of antioxidants, over consumption of antioxidants and increase in the production of prooxidants. Findings of this study with respect to total antioxidant capacity is consistent with that of Bogavac *et al.* (2017) in their study of preeclampsia and level of oxidative stress in the first trimester of pregnancy. They recorded significant decrease in the total antioxidant capacity of the study group compared to the control. In their study, they associated decreased levels of total antioxidant capacity in the case group to increased usage during the first trimester of pregnancy.

Oxidative stress index (OSI), a ratio of the total oxidant status to the total antioxidant status was increased in the placenta of the PIH suggesting the presence of oxidative stress in the placenta of the

https://doi.org/10.51374/annalsmls.2021.1.2.0041

subjects with PIH. In oxidative stress, there is an imbalance between reactive oxygen species and antioxidants (Montuschi *et al.*, 2007) in favour of oxidants which is evident in our data of subjects with pregnancy induced hypertension. The significant increase in oxidative stress index as found out in this study could be responsible for the significant rise of systolic and diastolic blood pressure in the PIH group.

Again, there was a significant negative correlation between oxidative stress index and parity suggesting that as parity increases, oxidative stress in the placenta decrease. The findings of this study with respect to parity contradicts that of Faegheh *et al.* (2016). In the study of maternal parity and blood oxidative stress in mother and neonate, Faegheh *et al.* (2016) reported a decreasing total antioxidant capacity with increasing parity; suggesting that oxidative stress increases with increasing parity. The difference in the findings of this study and that of Faegheh *et al.* (2016) may be due to the type or source of specimen. In this study, the specimen used was the placenta whiles in their study, maternal plasma was the specimen used.

Central to the pathogenesis of placental disorders is oxidative stress. It is considered a significant factor in the development of pregnancy complications such as preterm deliveries, still births, complications in infants, hydatidiform mole, preeclampsia, miscarriage in pregnancy and death (Saczko *et al.*, 2002b; Bogavac *et al.*, 2017). Various maternal, fetal, and environmental factors increase oxidative stress during birth (Noh *et al.*, 2014). Complications in pregnancies may develop due to the contributive effect of increased lipid peroxidation and reduced antioxidant activity (Orhan *et al.*, 2003).

In this study, a significant number of subjects in the PIH group had preterm deliveries and or still birth. This could have been the result of increased oxidative stress status and decrease antioxidant status (increased oxidative stress index) in the PIH group. Preeclampsia has been implicated as one of the reasons for induced preterm delivery (Ćebović *et al.*, 2013). Preterm delivery might not be entirely of benefit to the new born. Labour that occurs at term rather than preterm triggers an up-regulation of non-enzymatic antioxidant reserve that protects the newborn from the relative hyperoxia at delivery (Gyurkovits *et al.*, 2013).

Placental total antioxidant capacity was found to be a better marker of PIH than the other oxidant and antioxidant markers measured in this study. It might be a better marker because it reflects the combined action of all antioxidants in the system and the cooperation of these antioxidants to provide a better protection against ROS. Total antioxidant capacity is made up of different parameters of antioxidants such as cellular antioxidants (*acidum uricum*, bilirubin),non-enzymatic antioxidants (vitamins C, vitamin E, coenzyme Q) and catalase activity (Bogavac *et al.*, 2017). Aside total peroxide, all the other oxidative stress markers were significant with respect to being used as diagnostic markers of PIH. Placenta cholesterol was also found out not to be a good marker of PIH.

CONCLUSION

Placental malondialdehyde and oxidative stress index were found to be significantly increased in the PIH group whereas total antioxidant capacity and catalase were found to significantly low in the PIH group. This is indicative of an increased oxidative stress in the PIH group compared to the control group. Also, significant number of subjects in the PIH group had preterm deliveries and or still birth. Placental total antioxidant capacity was found to be a better marker of PIH than the other oxidative stress markers measured in this study. It is recommended that further studies be carried out with increased sample sizes to enhance the generalizability of these findings.

COMPETING INTEREST

Authors declare that they have no competing interests.

ACKNOWLEDGEMENTS

We are grateful to the Upper East Regional Hospital (Bolgatanga-Ghana) and all subjects for their kind collaboration.

https://doi.org/10.51374/annalsmls.2021.1.2.0041

REFERENCES

Bogavac M., Jakovljević A., Stajić§ Z., Nikolić A., Milošević-Tošić M., Dejanović J. and Lozanov-Crvenković Z. (2017) Preeclampsia and level of oxidative stress in the first trimester of pregnancy. *Vojnosanit Pregl* 74633–638.

Buege J.A. and Aust S.D. (1978) [30] Microsomal lipid peroxidation. *Methods in enzymology* 52302-310.

Burton G.J. and Jauniaux E. (2011) Oxidative stress. *Best Practice & Research. Clinical Obstetrics & Gynaecology* 25(3), 287-299.

Ćebović T.N., Marić D., Nikolić A. and Novakov-Mikić A. (2013) Antioxidant Status in Normal Pregnancy and Preeclampsia upon Multivitamin-Mineral Supplementation in the Region of Vojvodina. *International Journal of Bioscience, Biochemistry and Bioinformatics* 3(2), 138-144.

Dandana A., Gammoudi I., Ferchichi S., Chahed H., Limam H.B., Addad F. and Miled A. (2011) Correlation of Oxidative Stress Parameters and Inflammatory Markers in Tunisian Coronary Artery Disease Patients. *International Journal of Biomedical Science : IJBS* 7(1), 6-13.

Das B., Saha-Roy S., Das G.A., Lahiri T.K. and Das H.N. (2012) Assessment of Placental Oxidative Stress in Pre-Eclampsia. *The Journal of Obstetrics and Gynecology of India* 62 (1), 39–42.

Faegheh G., Fatemeh S., Akram R. and Mansour N. (2016) Maternal Parity and Blood Oxidative Stress in Mother and Neonate. *Biotech Health Sci.* 3(1).

Gyurkovits Z., Hracskó Z., Zimányi M., Varga I.S., Németh G., Pál A. and Orvos H. (2013) Comparison of oxidative stress markers in vaginal deliveries with or without epidural analgesia. *Redox Report* 18(1), 8-11.

Harma M., Harma M. and Erel O. (2005) Measurement of the total antioxidant response in preeclampsia with a novel automated method. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 118(1), 47-51.

Hubel C.A. (1999) Oxidative stress in the pathogenesis of preeclampsia. *Proc Soc Exp Biol Med* 222(3), 222-235.

Jain S., Nair A. and Shrivastava C. (2015) Evaluation of oxidative stress marker Malondialdehyde level in the cord blood of newborn infants. *International Journal of Scientific Study* 3(6), 73-76.

Kintiraki E., Papakatsika S., Kotronis G., Goulis D.G. and Kotsis V. (2015) Pregnancy-Induced hypertension. *Hormones (Athens)* 14(2), 211-223.

Koracevic D., Koracevic G., Djordjevic V., Andrejevic S. and Cosic V. (2001) Method for the measurement of antioxidant activity in human fluids. *Journal of clinical pathology* 54 (5), 356-361.

Kurlak L.O., Green A., Loughna P. and Broughton Pipkin F. (2014) Oxidative stress markers in hypertensive states of pregnancy: preterm and term disease. *Frontiers in Physiology* 5310.

Mehendale S., Kilari A., Dangat K., Taralekar V., Mahadik S. and Joshi S. (2008) Fatty acids, antioxidants, and oxidative stress in pre-eclampsia. *International Journal of Gynecology & Obstetrics* 100(3), 234-238.

Miyazawa T. (1989) Determination of phospholipid hydroperoxides in human blood plasma by a chemiluminescence-HPLC assay. *Free Radical Biology and Medicine* 7(2), 209-218.

Mohanty S., Sahu P.K., Mandal M.K., Mohapatra P.C. and Panda A. (2006) Evaluation of oxidative stress in pregnancy induced hypertension. *Indian Journal of Clinical Biochemistry* 101-105.

Montuschi P., Barnes P. and Roberts L.J., 2nd (2007) Insights into oxidative stress: the isoprostanes. *Curr Med Chem* 14(6), 703-717.

Myatt L. and Cui X. (2004) Oxidative stress in the placenta. *Histochemistry and cell biology* 122(4), 369-382.

Negre-Salvayre A., Auge N., Ayala V., Basaga H., Boada J., Brenke R., Chapple S., Cohen G., Feher J. and Grune T. (2010) Pathological aspects of lipid peroxidation. *Free radical research* 44(10), 1125-1171.

https://doi.org/10.51374/annalsmls.2021.1.2.0041

Noh E.J., Kim Y.H., Cho M.K., Kim J.W., Kim J.W., Byun Y.J. and Song T.-B. (2014) Comparison of oxidative stress markers in umbilical cord blood after vaginal and cesarean delivery. *Obstetrics & Gynecology Science* 57(2), 109-114.

Oghagbon S., Agu K., Omorowa F., Okolie N., Okwumabua M. and Omo-Erhabor J. (2016) Oxidative Stress Parameters as Markers of the different Trimesters in Normal Pregnancy. *J. Appl. Sci. Environ. Manage.* 20 (3), 567-571.

Orhan H., Onderoglu L., Yucel A. and Sahin G. (2003) Circulating biomarkers of oxidative stress in complicated pregnancies. *Arch Gynecol Obstet* 267(4), 189-195.

Pou K.M., Massaro J.M., Hoffmann U., Vasan R.S., Maurovich-Horvat P., Larson M.G., Keaney J.F., Meigs J.B., Lipinska I. and Kathiresan S. (2007) Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress. *Circulation* 116(11), 1234-1241.

Saczko J., Daczewska M., Marcinkowska A., ChwiŁKowska A., Saczko Z., OgorzaŁEk A. and Banas T. (2002a) Catalase (CT) Activity (SOD) in Placentas Complicated with Pregnancy Induced Hyperternsion (PIH). *Zoologica Poloniae* 4769-73.

Saczko J., Daczewska M., Marcinkowska A., ChwiŁKowska A., Saczko Z., OgorzaŁEk A. and Banas T. (2002b) Superoxide Dismutase Activity (SOD) in Placentas Complicated with Pregnancy Induced Hyperternsion (PIH). *Zoologica Poloniae* 4775-80.

Saxena S., Srivastava P.C., Mallick A.K., Das B., Thimmaraju K.V. and Dalmia K. (2016) Comparison of lipid profie and malondialdehyde with severity of blood pressure in pregnancy-induced hypertension. *International Journal of Medical Science and Public Health* 5(6), 1061-1065.

Sheena S.P. (2012) Comparative study of oxidative stress in pregnancy induced hypertension preeclampsia and eclampsia. *International Journal of Biomedical and Advance Research* 3 (11).

Shlafer M. and Shepard B.M. (1984) A method to reduce interference by sucrose in the detection of thiobarbituric acid-reactive substances. *Analytical biochemistry* 137(2), 269-276.

Sravanthi M.J., Sree G.R., Reddy D.P.G. and Subbaiah M.V. (2017) Pregnancy induced hypertension: A prospective study in pregnant women. *European Journal of Pharmaceutical and Medical Research* 4(12), 393-397.

Yanik M., Erel O. and Kati M. (2004) The relationship between potency of oxidative stress and severity of depression. *Acta Neuropsychiatrica* 16(4), 200-203.

Yeni E., Gulum M., Selek S., Erel O., Unal D., Verit A. and Savas M. (2005) Comparison of oxidative/antioxidative status of penile corpus cavernosum blood and peripheral venous blood. *International journal of impotence research* 17(1), 19-22.

Zahoorunnisa D., Swamy P.M.G. and Tembad M.M. (2014) Study Of Serum Lipid Profile, Malondialdehyde And Paraoxonase In Normal Pregnant Women And In Pregnant Women With Pre-Eclampsia. *International Journal of Pharmacy and Biological Sciences* 4 (2), 174-178.

ISSN 2773-8353