



## Antioxidant status of hypertensive pregnant Nigerian women and its effects on birth weight

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### Abstract

A study was conducted to evaluate the antioxidant status in hypertensive pregnancies compared with healthy normal pregnant and non-pregnant controls. All of them were evaluated for plasma non-enzymatic antioxidants (albumin, uric acid, carotene, glutathione, vitamin A, vitamin E and vitamin C) and antioxidant enzymes (Superoxide dismutase (SOD), Glutathione peroxidase and Catalase). The birthweights of babies from hypertensive pregnancies were also compared with that of normotensive pregnancies. It was observed that there was a significant decrease ( $P < 0.05$ ) in the activities of the antioxidant enzyme (except catalase) and the concentration of the non enzymatic antioxidants (except uric acid and vitamin E) in all the groups studied. Birthweights of babies of pregnant women with hypertension were found to be significantly lower ( $P < 0.05$ ) than that of normal controls. These results demonstrate that there is an imbalance between lipid peroxidation in hypertensive pregnancies and decreased antioxidant levels which may reflect an increased activity of free radicals. The data suggest that alterations in the plasma concentration of free radicals may have a causative function in reduction of plasma concentration of antioxidants, hence the involvement of antioxidants in the etiopathogenesis of hypertensive pregnancies.

**Keywords:** etiopathogenesis, lipid peroxidation, antioxidants, free radicals.

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### Introduction

Hypertensive pregnancy is high blood pressure that develops after the twentieth week of pregnancy and returns to normal after delivery with previously normal blood pressure [1].

Despite extensive research, the etiopathogenesis of hypertensive pregnancies remains unknown. It is widely accepted that endothelial cell dysfunction resulting in vascular permeability plays an important role in the pathophysiology of hypertensive pregnancies [2]. However, the precise cause of vascular endothelial dysfunction remains unknown. Free radicals which are highly reactive has been suggested to be promoters of maternal vascular malfunction [3]Antioxidants

may be of an interest in hypertensive pregnancies because of their ability to scavenge free radicals and their function as inhibitors of reactive oxygen species (ROS).

The involvement of antioxidants in hypertensive pregnancies in Nigerian women has not been fully elucidated. We therefore conducted a cross sectional study to compared the antioxidants status in normal with hypertensive pregnancies as well as to assess the involvement of these antioxidants in etiopathogenesis of hypertensive pregnancies and its effect on birthweights.

### **Subjects**

The study population consisted of one hundred and sixty (160) Nigerian women which are divided into four (4) groups. The first group is made up of eighty (80) hypertensive pregnant women in their 2<sup>nd</sup> and 3<sup>rd</sup> trimesters of pregnancy. The second group consisted of forty (40) normotensive pregnant women also in their 2<sup>nd</sup> and 3<sup>rd</sup> trimesters of pregnancy. They were age matched with blood pressure  $\leq 140/90$ mmHg without oedema or proteinuria with the first group. The first and second groups were monitored up to 3-6days postpartum. The third and the fourth groups are the normotensive (40) and hypertensive (40) non-pregnant women.

Hypertensive pregnancy was diagnosed when the blood pressure exceed 140/90mmHg after the 20<sup>th</sup> week of pregnancy. Before pregnancy the women did not suffer from chronic hypertension and after delivery their blood pressure returned to normal values without any pharmacological treatment but they have oedema and proteinuria.

Blood samples were collected into 10-ml ethylenediaminetetraacetic acid (EDTA) and centrifuged to obtain plasma. Plasma vitamin E, vitamin A and carotene were measured by High Performance Liquid Chromatography (HPLC) [4]. Plasma albumin was estimated by the dye binding method using Bromocresol Green (BCG) [5] while plasma uric acid was determined by the modified alkaline phosphotungstate method [6]. The concentration of plasma Vitamin C was measured by the 2-4dinitrophenylhydrazine method [7]. Superoxide dismutase activity was determined according to the method of [8]. Glutathione concentration was estimated by the method described by [9] while plasma activity of Glutathione peroxidase was determined by a modified method of [10]. Catalase activity was measured according to the method of [11]

The birthweight centile for each baby was computed, correcting for gestational age, sex, maternal parity and body mass index [12]

### **Statistical analysis**

Student's t-test was employed for the statistical analysis of data to compare each group. Results were expressed as means  $\pm$  Standard deviation. A P-value of  $< 0.05$  was considered statistically significant.

## Results

Table I: Demographic and pregnancy Data of Study Groups

Parameter	NNP	NP	HP	HNP	3-6days N	3-6days H
<b>Age (Year)</b>	29.00 ± 5.16	27.70 ± 4.98	31.50 ± 4.59	32.20 ± 4.56	31.80 ± 6.30	34.30 ± 6.82
Range	20 – 38	21 – 38	21 – 38	20-38	21 – 38	23 – 42
<b>Parity</b>	1.80 ± 1.24	1.60 ± 1.31	1.95 ± 3.52	1.60 ± 1.20	1.20 ± 0.90	1.90 ± 1.66
Range	0 – 4	0 – 4	0 – 4	0 – 4	0 – 4	0 – 4
<b>SBP (mmHg)</b>	99.50 ± 11.91	110.10 ± 10.50	163.20 ± 14.18	163.22 ± 16.89	103.20 ± 4.83	150.44 ± 4.71
Range	80 – 120	100 – 120	150 – 200	140-200	100 – 120	150 – 160
<b>DBP (mmHg)</b>	66.31 ± 11.05	66.12 ± 11.43	106.11 ± 10.95	109.50 ± 13.56	69.43 ± 3.16	97 ± 11.60
Range	60 -80	60 – 80	90 – 130	90 – 120	60 – 80	90 – 130
<b>Proteinuria (g/l)</b>	-	-	2.00 ± 0.89	-	-	1.55 ± 0.35
<b>Oedema</b>	-	-	+++	-	-	-
<b>Birthweight (kg)</b>	-	3.45 ± 1.02	2.11 ± 0.05	-	-	-
Range	-	3.20 – 4.55	1.51 ± 0.01	-	-	-
<b>Birthweight Centile</b>	-	50.00 ± 5.33	30.32 ± 5.22	-	-	-

Data are presented as mean ± SD.; NNP – Normotensive non pregnant; NP – Normotensive pregnant; HP – Hypertensive pregnant; HNP – Hypertensive non pregnant; 3-6day NP – 3-6days normotensive postpartum; 3-6daysHP – 3-6days hypertensive postpartum

Table II: Plasma antioxidants in the Study Groups

Parameter	NNP	NP	HP	HNP	3-6days N	3-6days H
<b>Non-enzymatic antioxidants</b>						
Albumin (g/l)	45.80 ± 9.80	34.25 ± 2.26	30.40 ± 1.54	41.10 ± 5.97	50.50 ± 4.22	51.10 ± 2.33
Uric acid (g/l)	0.21 ± 0.05	0.29 ± 0.22	0.22 ± 0.15	0.20 ± 0.02	0.29 ± 0.10	0.30 ± 0.10
Carotene (µmol/l)	0.50 ± 0.10	0.49 ± 0.20	0.20 ± 0.15	0.45 ± 0.11	0.48 ± 0.18	0.40 ± 0.09
Glutathione (µmol/l)	2.30 ± 0.31	2.33 ± 0.11	2.00 ± 0.15	2.23 ± 0.60	2.35 ± 0.10	2.21 ± 0.30
Vitamin A (µmol/l)	2.25 ± 0.99	2.50 ± 0.89	1.15 ± 0.51	2.00 ± 0.61	2.23 ± 0.94	2.23 ± 0.86
Vitamin C (µmol/l)	94.11 ± 10.22	98.20 ± 11.55	68.90 ± 9.55	78.50 ± 6.11	92.20 ± 5.18	75.30 ± 5.35
Vitamin E (µmol/l)	10.33 ± 2.14	10.11 ± 2.14	15.20 ± 3.11	12.35 ± 2.18	10.23 ± 2.00	12.00 ± 2.00
<b>Enzymatic antioxidants</b>						
SOD (µg/l)	4.33 ± 0.71	4.00 ± 0.02	1.24 ± 0.02	3.11 ± 0.08	4.23 ± 0.05	3.55 ± 0.11
GPx (µg/l)	0.67 ± 0.10	0.95 ± 0.11	0.36 ± 0.17	0.42 ± 0.09	0.90 ± 0.09	0.59 ± 0.17
Catalase (µ/mg)	87.45 ± 11.31	80.55 ± 12.38	100.30 ± 20.40	90.30 ± 10.41	82.11 ± 9.33	85.38 ± 11.39

Data are presented as mean ± SD; NNP – Normotensive non pregnant; NP – Normotensive pregnant; HP – Hypertensive pregnant; HNP – Hypertensive non pregnant; 3-6day NP – 3-6days normotensive postpartum; 3-6daysHP – 3-6days hypertensive postpartum; SOD – Superoxide dismutase; GPx – Glutathione peroxidase

Table 1 describes the demographic and pregnancy data of the study groups. The mean maternal age and parity of the hypertensive group did not significantly ( $P > 0.05$ ) differ from those of the normotensive group while there was a significant ( $P < 0.05$ ) difference in systolic and diastolic blood pressure in both groups. The values of plasma non-enzymatic antioxidants (except uric acid and vitamin E) concentrations and the activities of enzymatic antioxidant (except catalase) were significantly lower ( $P < 0.05$ ) in hypertensive groups compared to both normal pregnancy

and non-pregnant controls ( $P < 0.05$ ). No significant differences were observed between non-pregnant and normal pregnancy group.

There was a highly significant trend for decreasing plasma antioxidants (except uric acid and Vitamin E) concentration from non-pregnant, to normal pregnant and hypertensive pregnancy. The obtained results showed differences in birth weight of babies between hypertensive and normal pregnancy.

## **Discussion**

We observed a comparatively lower non enzymatic antioxidants concentration and enzymatic antioxidant activities in hypertensive pregnant Nigerian women than in their normotensive counterparts. The levels and activities of these antioxidants were significantly decreased ( $P < 0.05$ ) in normal pregnant women and women with hypertensive pregnancy compared with non-pregnant women. Reduced maternal circulation of antioxidants in normal pregnancies has been associated with increased oxidative stress and lipid peroxidation [13, 14].

Lower plasma vitamin C and A concentrations were observed in women with hypertensive pregnancy in this study. This conforms with the reports of [15, 16]. This significant reduction in the plasma concentration of these Vitamins may be attributed to their increased utilization in removing excess free radicals.

This study has also shown the plasma albumin to be significantly low in hypertensive than normotensive pregnancy. This observation had been documented earlier [17, 18].

There was no significant difference in the mean values of uric acid in all the groups studied. Our study agrees with [19]. However, this was in contrary to the findings of other workers who reported raised plasma level of uric acid in hypertensive pregnancy [20, 21]. This might be due to the effect of hypertensive pregnancy on the renal system in early pregnancy which may be minimal to produce any detectable change in the plasma levels of uric acid [19]

The highly significant decrease in plasma glutathione levels and glutathione peroxidase activity in hypertensive subjects conforms with previous report [22]. This decrease in glutathione peroxidase might be due to the insufficient antioxidant defense mechanism as a result of oxidative stress associated with hypertensive pregnancy.

There was a significant fall ( $P < 0.05$ ) in carotene levels in hypertensive pregnancy in comparison with normotensive pregnancy, postpartum and non pregnancy. Our study agrees well with the studies of [23, 24] who noted that the mean plasma carotene concentration among preeclamptic women were 40 percent lower as compared with the mean concentration in normotensive pregnant West African women. This lower circulating carotene levels might be due to an increased consumption of this antioxidant in the face of enhanced free radical activity.

Several studies have shown the extent to which plasma Vitamin E concentrations are altered in hypertensive versus normotensive pregnancy. Our finding of increased Vitamin E concentration in hypertensive pregnancies is consistent with results from previous studies [16, 25]. This elevated Vitamin E in hypertensive pregnancy compared with normotensive pregnancy women might be attributed to decreased absorption of Vitamin E from the gut as a result of vasoconstriction in hypertensive pregnancies. Another possibility is an altered placental physiology such as placental infarction, proliferation of the cytotrophoblast and thickened of the trophoblastic basement membrane.

In the present study, activity of catalase is significantly higher in hypertensive than in normal pregnancy, 3-6days postpartum and non pregnant state. This is in agreement with the reports of [26]. This increase in catalase activity may be due to the activation of antioxidant enzymes resulting from an uncontrolled increase of Reactive Oxygen Species (ROS) seen in hypertensive pregnancy.

The obtained results showed a significantly lower activity of plasma SOD in hypertensive when compared with normotensive pregnancies. Similar observation has been made by [27]. From the results obtained from this study, the birth weight of babies of hypertensive pregnant women were found to be significantly reduced than that of the normotensive pregnant women as the birthweight centile was below 50% in hypertensive pregnancies. Similar result has been reported by [28]. Hence, plasma antioxidants status of babies of hypertensive pregnant women may be altered. This needs to be investigated.

The low levels of plasma non-enzymatic antioxidant, which correlates positively and significantly with the high blood pressure in hypertensive pregnancies coupled with the low activities of antioxidant enzymes suggests that reduced plasma levels of antioxidants, may be very likely to be an aetiological factor of hypertensive pregnancies.

In view of the abnormally low plasma antioxidants in hypertensive pregnancies, foods supplementation of these antioxidants can be a promising prophylactic strategy for prevention and management of hypertensive pregnancies.

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