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Plasma thiol levels in pregnancy induced hypertension in Nigerians

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Abstract

The association between plasma thiol (homocysteine, cysteine and glutathione) levels and Pregnancy Induced Hypertension (PIH) in Nigerian women was investigated. The levels of cysteine and homocysteine in pregnancy induced hypertensive subjects were significantly higher ($P < 0.05$) than the normotensive subjects and plasma glutathione was lower in PIH than in normotensive pregnancy. Postpartum levels of cysteine as well as homocysteine were lower in PIH and normotensive pregnancy when compared with the corresponding postpartum values. However, glutathione levels were significantly higher $P < 0.05$ in normotensive non - pregnant as well as in normotensive women compared with hypertensive women, during as well as after pregnancy. Our findings indicate that the alterations in plasma thiol levels might be related with the pathogenesis of pregnancy Induced hypertension in Nigerian pregnant women.

Key words: Thiol, pregnancy induced hypertension, pathogenesis, normotensive, hypertensive.

INTRODUCTION

Homocysteine is an amino acid formed from the metabolism of the essential amino acid, methionine which is abundant in proteins of animal origin. Increased plasma levels of total homocysteine has been linked with an increased risk of endothelial dysfunction and vascular diseases such as preeclampsia [1, 2], intrauterine growth restriction and abruption placenta [3], stillbirth [4] and miscarriage [5].

Glutathione, an intracellular tri-peptide of the amino acids cysteine, glycine and glutamic acid is the most abundant thiol-based antioxidant compound found in living animal and plant tissues. Glutathione participate directly in the neutralization of free radicals, reactive oxygen compounds and maintains exogenous antioxidants such as vitamins C and E in their active forms [6].

Glutathione also plays a role in the detoxification of many xenobiotics, it helps in the storage and transport of cysteine and maintain the reduced state of proteins and thiols [7].

Cysteine is a sulfhydryl amino acid which is present in many proteins and because it is a sulfur-based amino acid, cysteine acts as an antioxidant in the body. The availability of cysteine makes it the rate-limiting substrate for the synthesis of glutathione within the cell. The sulfhydryl (thiol) group (SH) of cysteine that serves as proton donor and is responsible for the biological activity of glutathione [8].

Pregnancy Induced Hypertension (PIH) is a complication of pregnancy characterized by increasing hypertension, proteinuria and oedema developing after the 20th week of pregnancy. PIH is the leading cause of fetal and maternal morbidity and death in Nigeria and many other countries in the world [9-11]. It may lead to increased risk of fetal growth restriction and induced premature delivery due to disease progression on the maternal or fetal side [12, 13].

The cause of PIH is unknown [14], several factors have been shown to be involved [15]. PIH has also been linked to dysfunction of vascular endothelium [16]. Recent studies have shown an association between sulfur containing amino acids [17-19]. Therefore, plasma thiol concentrations might be relevant because of their relationship with vascular diseases [20, 21]. No much study has been done on the thiol status of hypertensive pregnant Nigerian women. We therefore investigated the association between plasma thiol concentrations and hypertension in Nigerian pregnant women.

MATERIALS AND METHODS

The present study was carried out in the Department of Chemical Pathology, Obafemi Awolowo University Teaching Hospital, (OAUTH) Ile-Ife, Osun State, Nigeria. The study included both hypertensive and normotensive pregnant women attending antenatal clinics in Out Patients Department (OPD) of OAUTH. All the subjects were ranging 20-45 years. The subjects were divided into two groups.

Group 1 included twenty subjects of normal pregnant women that serve as controls who did not have any history of hypertension. Group 2 are made up of thirty (30) pregnancy induced hypertensive pregnant women. All subjects were monitored up to 3-6 days after delivery in both groups.

Blood Sampling

Blood samples were drawn from all the subjects following a fast of 12 hours. Plasma was separated by centrifuging the blood at 3000rpm for 10 minutes at 4°C. This plasma was used for the estimation of cysteine, homocysteine and glutathione.

Biochemical Assay

Glutathione level in plasma was estimated by the method of [22]. Determination of homocysteine and cysteine were carried out using High Performance Liquid Chromatography [21].

Statistical Analysis

Data obtained from the present study were presented as mean value \pm SD. The statistical significance was evaluated by student's "t" test.

RESULTS AND DISCUSSION**Table 1: Clinical characteristics of the study groups**

Characteristics	Hypertensive pregnant women	Normotensive Pregnant women	P-Value
Number of women	30	20	NS
Age (Years)	31.32 (20-45)	31.32 (20-45)	NS
Gestational age (Weeks)	34 (28-40)	34 (28-40)	NS
Systolic Blood Pressure (mmHg)	158.20	101.75	P<0.05
Diastolic Blood Pressure (mmHg)	105.60	62.00	P<05

Table 2: Plasma Thiol levels in hypertensive and normotensive pregnant women

Parameters	Hypertensive Pregnant Women	Normotensive Pregnant Women	3-6days Postpartum Hypertensive Women	3-6days Postpartum Normotensive Women	Non-Pregnant Women
Glutathione ($\mu\text{mol/l}$)	6.72 \pm 1.89	10.25 \pm 1.90	4.11 \pm 1.38	13.10 \pm 2.38	14.32 \pm 3.11
Total homocysteine ($\mu\text{mol/l}$)	15.80 \pm 1.62	5.80 \pm 1.54	13.20 \pm 4.32	9.24 \pm 1.18	10.23 \pm 1.34
Cysteine ($\mu\text{mol/l}$)	40.55 \pm 9.30	20.11 \pm 10.18	28.22 \pm 5.83	21.01 \pm 9.81	20.66 \pm 6.30

*P-Value<0.05

Characteristics of the hypertensive and normotensive women are summarized in Table 1. There were no significant differences between the groups as regarding ages, number of women and gestational age. However, significantly higher values were found for Systolic Blood Pressure and Diastolic Blood Pressure in hypertensive patients.

Comparing hypertensive patients with normotensive pregnant controls, the first group showed significantly lower plasma concentrations of glutathione while significantly higher values were seen in hypertensive patient 3-6 days postpartum. When comparing the hypertensive pregnant women with normotensive pregnant controls, significantly lower values were observed for total homocysteine. Conversely, significantly lower values in hypertensive patient 3-6days after delivery was observed for total homocysteine.

Women with hypertension showed significantly higher values for cysteine than the corresponding values for controls. Plasma cysteine were significantly lower in hypertensive patients 3-6 days post partum compared with hypertensive pregnant women.

Pregnancy Induced Hypertension is one of the major causes of maternal and fetal mortality in Nigeria. The concentrations of Thiols (glutathione, cysteine and homocysteine) in the present study were found to be significantly higher in non-pregnant women than in normotensive pregnant women. The alterations in plasma steroid concentration during pregnancy might be a

contributory factor to the lowering of these thiols in pregnancy [23]. Similar observation has been reported [24].

The high concentration of homocysteine observed in hypertensive pregnancy might be as a result of a decreased activity of one of the enzymes responsible for the remethylation of homocysteine to methionine [25] or pathological process of haemoconcentration observed in this condition [24]. The results of this study also showed that homocysteine and cysteine in hypertensive pregnant women were significantly higher than in normotensive pregnancy and 3-6 days postpartum normotensives and non-pregnant controls. This is in agreement with the reports of many other workers [26-28]. Increased plasma level of homocysteine and cysteine indicate an increased risk of cardiovascular diseases. Infact, homocysteine has been identified as an independent risk factor for atherosclerotic disease in coronary, cerebral and peripheral vessels [29]. Homocysteine has been suggested to exacerbate conventional risk factors of cardiovascular diseases, such as smoking or high cholesterol [30]. Homocysteine may therefore augment clotting effects or exert a toxic effect on the endothelium and these might account for the genesis of vascular diseases.

The significantly ($P<0.05$) low level of glutathione observed in hypertensive pregnant women in this study is in agreement with previous reports [31, 32]. Depletion in plasma level of glutathione has also been linked with lipid peroxidation [33], which occurs as a result of hypertension and thus the production of free radicals that damage the endothelial tissues. The roles of glutathione in neutralizing free radicals and reactive oxygen compounds thereby protecting macromolecules against oxidative damage is clearly evident from our findings since the antepartum and postpartum levels of glutathione were significantly higher in normotensive women compared with hypertensive women. The decreased glutathione levels in hypertensive pregnancy might be due to disturbances in the synthesis of glutathione in this condition. This indicates that glutathione might be a contributory factor to hypertension in pregnancy.

CONCLUSION

From our results, it is evident that the levels of homocysteine and cysteine are significantly higher while glutathione is lower in hypertensive pregnancy. Antepartum levels of homocysteine as well as cysteine were higher in hypertensive than in normotensive pregnancy. The hyperhomocystemia and lowered level of glutathione are transitory abnormalities which corrected themselves after delivery. Thus, we conclude that Pregnancy Induced Hypertension is associated with changes in thiol levels in Nigerian women.

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