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Proteinuria And Osmotic Fragility Of Erythrocytes In Anaemic Pregnant Hypertensives

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ABSTRACT

Hypertensive disease in pregnancy is known to be a leading cause of mortality. Some like preeclampsia are pregnancy-induced and may be complicated by cardiovascular and hematologic changes. The present study was designed to assess the incidence and severity of proteinuria (indicative of preeclampsia) in anaemic hypertensive pregnant women. Erythrocyte fragility was also determined as a probable hematologic change which could cause anaemia.

Thirty-four pregnant women in the third trimester of pregnancy were used for the study. Urine protein was estimated using the biuret reaction while erythrocyte fragility was determined through haemolysis studies.

Results indicate that the hypertensive subjects were proteinuric and their urine albumin concentration was significantly higher ($P < 0.001$) than that of the normotensive subjects. Also percentage erythrocyte haemolysis in the hypertensive subjects was significantly higher ($P < 0.001$).

These results imply a high association of proteinuria with hypertension in pregnancy, and the hypertension may cause erythrocytes to become fragile leading to haemolysis and anaemia.

Key Words: Proteinuria, Erythrocyte Fragility, Preeclampsia.

INTRODUCTION

Hypertension in pregnancy is considered a serious condition since it could result in eclampsia which is known to be a dangerous condition for both mother and baby, sometimes with fatal results.

Proteinuria is generally considered a reliable sign of preeclampsia apart from being one of the signs by which the disorder is defined, and it has been reported that the degree of proteinuria relates to the severity of the condition^{1,2}. Proteinuria has been associated with higher rates of maternal and fetal complications among preeclamptic women, thus detecting proteinuria has been accepted as an integral part of management of preeclampsia and other hypertensive disorders of pregnancy^{3,4,5}.

Although several classification schemes have been proposed to aid the clinical recognition of

preeclampsia many workers simply classify preeclampsia as a blood pressure of 140/90-mm Hg. and above plus proteinuria and/or oedema in pregnancy^{6,7}. The mean arterial pressure (MAP) is often considered a more appropriate physiologic index of total peripheral resistance which is directly proportional to the blood pressure. MAP in pregnant women is known to vary with the duration of pregnancy becoming lowest in the middle trimester and highest in the third trimester. Thus in the second trimester an MAP of 90mm Hg or above is regarded as hypertensive while an MAP of 105mm Hg is used as the dividing line between normotension and hypertension in the third trimester⁸.

Cardiovascular and hematologic changes in the mother are associated with preeclampsia. The hematologic changes include an alteration of the coagulation mechanism and haemolysis⁹, and they appear to be related to the severity and duration of the disorder. Anaemia is a common occurrence during pregnancy especially in the developing countries, the anaemia could be a haemolytic one caused by the fragmentation or rupturing of the erythrocytes as they attempt to pass through arterioles partially occluded by a damaged endothelium. The condition becomes more likely in the presence of weak and fragile erythrocytes.

The present study was therefore designed to assess the incidence and severity of proteinuria in anaemic hypertensive pregnancies, and to determine erythrocyte fragility in such individuals in an attempt to establish probable causes of observed anaemia.

MATERIALS AND METHODS

Subjects

Pregnant women attending ante-natal clinics at the Lagos University Teaching Hospital were used for the present study. The study group consisted of 15 hypertensive pregnant women and 19 normotensive pregnant women all in the third trimester of pregnancy. Those classified as hypertensive had blood pressures greater than 140/90mm Hg. and mean arterial pressures above 105 mm Hg while those classified as normotensive had diastolic pressures lower than 85 mm Hg. and mean arterial pressures below 105 mm Hg. These subjects were free of malaria and had no previous history of hypertension or diabetes.

Protein Estimation

A sample of early morning urine was obtained for protein (albumin) estimation. The biuret method of protein estimation¹⁰ was used to estimate albumin concentration in the urine samples. This method is based on the fact that the CO-NH- group of proteins form a purple complex with copper ions in an alkaline medium. Since all the proteins contain the peptide bond, the method is fairly specific and there is little interference from other compounds.

Erythrocyte Fragility

The method used in determining the erythrocyte fragility was that described by Dacie and Lewis¹¹. This method is based on the fact that normal red blood cells shrink when suspended in solutions with osmotic pressures greater than that of plasma, and when in solutions with lower osmotic pressures, they swell, becoming spherical rather than disk-shaped and eventually rupture and lose their haemoglobin. The haemoglobin of the haemolysed red blood cell dissolves in the solution colouring it red. The intensity of the colouration in the solution is proportional to the incidence of haemolysis. However, weak and fragile erythrocytes may haemolyse even in hypertonic solutions, and the fragility of erythrocytes can therefore be assessed by determining the osmotic pressure at which the erythrocytes being to haemolyse.

RESULTS

Table I shows the clinical data of the subjects as regards age, weight, gestational age and incidence of anaemia. Haemoglobin level was significantly ($P<0.001$) lower in the hypertensive subjects than in the normotensives.

Results from the study establish a clear difference in the blood pressures of normotensive and hypertensive subjects. The systolic, diastolic and mean arterial pressures were significantly higher ($P<0.001$) in the hypertensives than in the normotensives as shown in table II.

Urine protein concentration in the hypertensive pregnant subjects was also significantly higher than what obtained in the normotensives ($P<0.001$) as presented in table III and fig. 1.

It was also observed that erythrocytes in the blood of pregnant hypertensives were more fragile than those in the blood of the normotensives. Table IV and figs. 2 and 3 show that at osmotic concentrations slightly lower and also higher than that of plasma (0.6 - 1.2gm% NaCl) percentage erythrocyte haemolysis was significantly higher in the hypertensives than in the normotensives ($P<0.001$). Haemolysis at these concentrations is indicative of erythrocyte fragility.

Table I
Clinical Data of Pregnant subjects Studied

	Normotensive group (n = 19) Mean ± S.E.M.	Hypertensive group (n = 15) Mean ± S.E.M.	P value
Age (years)	29.2 ± 4.8	29.7 ± 2.02	>0.05 (NS)
Weight (Kg)	72.36 ± 15.6	82.63 ± 11.66	>0.05 (NS)
Gestational Age (weeks)	30.2 ± 4.28	30.26 ± 4.4	>0.05 (NS)
Haemoglobin Conc. in blood (g/dL)	12.72 ± 0.62	10.14 ± 0.35	1 <0.001 (S)

NS = Not Significant
S = Significant

Table II
Blood Pressure Measurements in Normotensive and Hypertensive Pregnant Women

Blood Pressure (mm Hg)	Normotensive group (n = 19) Mean ± S.E.M.	Hypertensive group (n = 15) Mean ± S.E.M.	P value
Systolic blood Pressure	111.58 ± 6.02	151 ± 12.3	1 <0.001 (S)
Diastolic blood Pressure	67.89 ± 7.1	92.67 ± 7.03	1 <0.001 (S)
Mean arterial Pressure	84.04 ± 1.41	112.24 ± 2.05	1 <0.001 (S)

S = Significant

Table III
Comparison of Urine Albumin in Normotensive and Hypertensive Pregnant Women

Blood Pressure (mm Hg)	Normotensive group (n = 19) Mean ± S.E.M.	Hypertensive group (n = 15) Mean ± S.E.M.	P value
Mean arterial Pressure (mm Hg)	84.04 ± 1.41	112.24 ± 2.05	1 <0.001 (S)
Concentration of albumin in urine (g/L)	1.27 ± 0.53	2.68 ± 0.45	1 <0.001 (S)

S = Significant

Table IV
Percentage Haemolysis of Erythrocytes in Normotensive and hypertensive Pregnant Women

Percentage Concentration of NaCl (gm %)	Mean percentage Haemolysis (Mean ± S. E. M)		P Value
	Normotensive group (n = 19)	Hypertensive group (n = 15)	P value
0.0	100.0 ± 0.0	100.0 ± 0.0	P > 0.05 (NS)
0.1	97.5 ± 3.95	97.8 ± 3.96	P > 0.05 (NS)
0.2	88.6 ± 12.04	92.9 ± 5.17	P > 0.05 (NS)
0.4	49.1 ± 15.5	65.9 ± 9.9	P < 0.05 (S)
0.6	2.5 ± 4.02	31.4 ± 15.3	P < 0.001 (S)
0.9	0.6 ± 2.15	19.0 ± 14.3	P < 0.001 (S)
1.0	0.4 ± 1.9	16.4 ± 9.6	P < 0.001 (S)
1.2	0.4 ± 1.8	16.4 ± 9.7	P < 0.001 (S)

NS = Not Significant
S = Significant

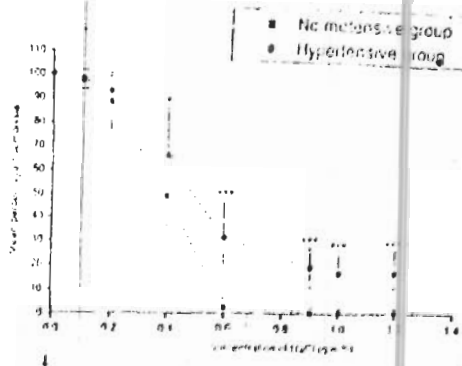


Fig. 3 mean erythrocyte fragility curve in normotensive and hypertensive pregnant women (* p < 0.05, *** p < 0.01).

DISCUSSION

The present work showed the presence of proteinuria in the hypertensive pregnant women studied thus confirming them as pre-eclamptic. This observation is similar to those from some earlier studies.^{12,13} High levels of albumin in urine could be due to some pathological damage to the glomerular cells causing an increase in the permeability of these cells. According to Paternoster et al¹³ the incidence of high urine albumin may also be due to tumours from endothelial tissues of glomerular blood vessels with a generalised increase in capillary permeability which would lead to an increase in protein filtration at the glomerulus. The high levels of albumin in the urine of the studied hypertensive pregnant women could also be due to an increased production of a vascular endothelial growth factor as earlier observed by Sharkey et al¹² who reported that this growth factor contributes to the leakage of proteins into the surrounding tissues causing oedema.

Results of the present study also showed higher haemolysis and fragility in the red blood cells of the hypertensive subjects than that observed in the normotensives. Similar results were reported by Ozan et al¹⁴ who investigated possible correlation between blood pressure, proteinuria, and erythrocyte fragility during pre-eclampsia and eclampsia. They concluded that the observed increased fragility was probably due to an elevation in peroxide and free radical levels in pre-eclamptic pregnancies since pre-eclampsia is believed to be caused by an imbalance between oxidants and antioxidants in the circulation.

The increased haemolysis may also be responsible for the reduction in the haemoglobin concentration of the hypertensive subjects. A similar reduction in

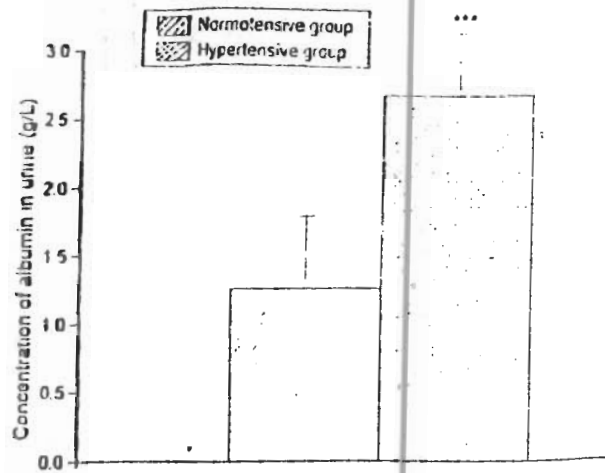


Fig. 1: Urine albumin concentration in normotensive and hypertensive pregnant women. (***) p < 0.001.

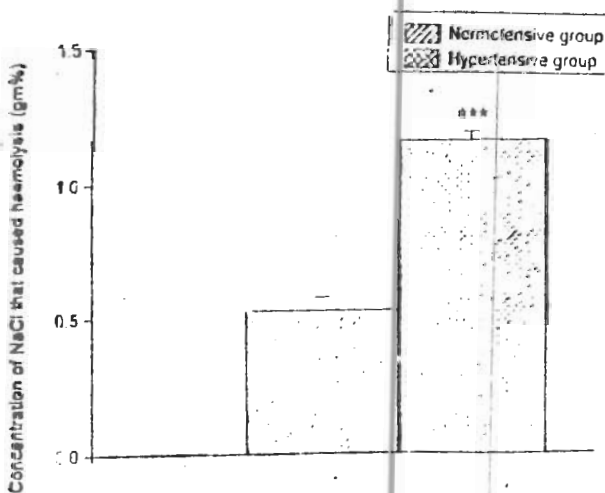


Fig. 2: Percentage sodium chloride concentration that caused haemolysis in normotensive and hypertensive pregnant women. (***) P < 0.001.

haemoglobin level of preeclamptic women was reported by Odar-Cederlof et al¹⁵. In pregnancy haemoglobin levels below 11.0 gm % represent anaemia⁸. The present work therefore confirms anaemia in the hypertensive pregnant women studied (10.1 gm % haemoglobin).

It is clear from the present study that proteinuria is highly associated with hypertension in pregnancy, and indeed some normotensive pregnant women are also proteinuric. Also preeclampsia may cause red blood cells to become weak and fragile leading to haemolysis and anaemia. The present observations and further research into the mechanisms through which hypertension may cause erythrocyte fragility will help in the development of drugs that will counteract such actions, and hence reduce the incidence of anaemia in pregnancy. It will also enable the clinician to achieve better management of preeclamptic patients thus reducing the high incidence of mortality associated with the disease.

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