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# Assessment of Total Protein, Albumin, Creatinine and Aspartate Transaminase level in Toxemia of Pregnancy

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Preeclampsia is majorly a clinical disorder of pregnancy (occurring after 20 weeks of gestation in previously normotensive women) with unknown pathophysiology and associated organ dysfunctions. This study determined the biochemical changes associated with preeclampsia in the serum and urine. Blood pressure, serum total protein, albumin, creatinine and aspartate transaminase level and urinary protein were assessed (using standard methods) in 105 primigravidae. There was no significant difference ($p>0.05$) in booking systolic and diastolic blood pressure but significant differences ($p<0.05$) existed between systolic and diastolic blood pressure of preeclamptic patients and controls. Also, 9 (10.1%) out of 89 that completed the study had preeclampsia, 3 (3.4%) had pregnancy induced hypertension only while 77 (86.5%) remained normotensive. Serum total protein (50.11±3.33), albumin (22.67±1.22) and globulin (27.44±3.78) levels were found to be significantly low ($p< 0.05$) in preeclampsia as compared to the control (69.33±1.5, 37.78±2.59 and 31.56±3.25, respectively) while serum Aspartate Transaminase (27.11±4.73) and creatinine (90.44±1.74) levels were found to be significantly higher ($p<0.05$) in preeclampsia than controls (8.56±3.17 and 62.67±1.58, respectively). The outcome of the pregnancy shows that two patients had abortion, one had preterm delivery and one had intrapartum eclampsia. Conclusively, results of hematologic and biochemical parameters should be considered for the timing delivery of women with pre-eclampsia as indicated by high levels of AST, blood pressure greater than or equal to 140/90 mmHg and proteinuria of ≥300 mg/24 h.

**Key words:** Preeclampsia, hypertension, proteinuria, hypoproteinemia, pregnancy

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## INTRODUCTION

Preeclampsia (PE) is a clinical condition characterized by systolic and diastolic hypertension (systolic and diastolic blood pressure of ≥140 and 90 mmHg respectively, on two occasions, at least 6 h apart) and proteinuria (protein excretion of ≥300 mg in a 24 h urine collection (a dipstick of ≥++), or a random urine protein dipstick test of ≥+ occurring in a previously normotensive woman after 20 weeks of gestation (Redman and Sargent, 2005; Sibai *et al*., 2005). It is a major cause of maternal and neonatal morbidity, leading to iatrogenic prematurity because the known definitive treatment is delivery of the baby and placenta (Hofmeyr and Belfort, 2009). It complicates up to 10% of pregnancies in the developing countries (Grill *et al*., 2009) and responsible for about 60,000 maternal deaths every year, mainly in poor countries due to lack of or inadequate emergency care (WHO, 2005) and probably reflecting nutritional status amongst people in developing countries.

The pathogenesis of preeclampsia involves interaction of genetic, immunologic and environmental factors. The early stage of preeclampsia is asymptomatic and this is characterized by placenta abnormality during the first trimester with consequent placental insufficiency and release of placental materials into the maternal circulation. The later stage of preeclampsia is characterized by signs and symptoms suggestive of multi organ involvement and these include hypertension, proteinuria, hemolysis, raised liver enzymes, low platelets and eventually eclampsia. The characteristic clinical features (proteinuria and hypertension) is a consequent of glomerular endotheliosis.

Vasoconstriction occurs in women with overt preeclampsia and thus has multiple organ dysfunctions secondary to reduced perfusion and evidence of activation of coagulation cascade and loss of endothelial integrity (Masse *et al*., 2002). Thus, there is associated renal damage resulting in proteinuria, which has been described as a dysfunction of pre-eclampsia (DMPE, 2002).

The pathophysiology of preeclampsia is yet to be fully understood but progress has been made during the past years for early detection and prediction of high risk women using biochemical, ultrasonographic and genetic markers. No single marker has been established to have high predictive value, biochemical markers allows for easy grouping of preeclamptic patients into different categories based on the severity of symptoms and outcome of pregnancy and therefore improve its management (Von Dadelszen *et al*., 2004). With the use of markers, early disease detection is enhanced in asymptomatic pregnant women that are at risk of developing pre-eclampsia during pregnancy (Grill *et al*., 2009).

For many years past, quantitative analysis of protein in a timed-urine collection has been the gold standard (Hofmeyr and Belfort, 2009). A 24 h urine specimen collection has generally been used for the analysis, but some researchers had also suggested the use of a 12 and 2 h urine collections (Abebe *et al*., 2008). However, due to problems of complete 24 h urine collection, urinary protein:creatinine ratio was used by some researchers (Haas *et al*., 2003). While some of these researchers found this to be useful in determining pathologic proteinuria in pre-eclampsia, others have contrary opinion (Durnwald and Mercer, 2003). The use of proteinuria as a predictive marker and measure of the severity of pre-eclampsia and adverse outcomes for mothers by some researchers (Von Dadelszen *et al*., 2004), prompted the need to embark on this research and also to determine associated biochemical changes in preeclampsia.

## MATERIALS AND METHODS

This study was a longitudinal and carried out within a period of eighteen months (January 2011-July 2012) using primigravidae patients that attended antenatal clinic of Badagry general hospital. A total of 105 patients were recruited on their booking day in preparation for antenatal care. Informed consent was sought for and obtained from all individuals recruited for the study. The gestational age of each of the pregnancies was determined using the first day of their last menstrual period and confirmed using pelvic ultrasonographic studies of all the patients. They were divided in to two groups. Group one comprises of those that have increase systolic pressure of more than 30 mmHg and diastolic pressure of more than 15 mmHg above their booking blood pressure for two consecutive clinic attendance and proteinuria of ≥300 mg in 24 h while group two comprises of those with normal systolic and diastolic blood pressure and this serve as controls.

Excluded from the study were pregnant women first seen after the 20th week of pregnancy, women having multiple gestations, women with pre-existing hypertension, diabetes mellitus and features of renal disease and those who did not give consent. Those included in the study were monitored and followed up till delivery. Those with pregnancy-induced hypertension were divided according to gestation into four (20-24, 25-29, 30-34 and ≥34 weeks).

At each clinic visit the blood pressure of the patients and controls was determined using mercurial sphygmomanometer in the sitting position with the arm rested. The first and fifth phases of Korotkof sounds were

used for systolic and diastolic respectively. Hypertension was defined as systolic and diastolic blood pressure of ≥140 and 90 mmHg, respectively (Chobanian *et al*., 2003), on two occasions, at least 6 h apart.

Five milliliters (5 mLs) of blood was collected from each participant, with minimum stasis, using pyrogen-free needles and disposable plastic syringes and allowed to clot. The clotted blood samples were separated in a centrifuge at 4,000 rpm for 5 min. All the sera samples were kept at 10°C until ready for analysis.

Serum creatinine, total protein and albumin were measured by methods described by Jaffe (1886), Kingsley (1939) and Doumas *et al*. (1971) respectively in both PE and control. Total globulin was computed from the difference between total serum protein and albumin level. Serum AST activity was determined using the method described by Reitman and Frankel (1957).

A dipstick urine measurement for protein was performed on urine specimen collected from the patient on the clinic days. Testing was performed with multistix reagent strips (Bayer). Proteinuria was classified semiquantitatively as absent if testing with a dipstick showed no protein or trace levels (level below 300 mg $L^{-1}$); low grade if the dipstick showed a value of 1+ or 2+(level between 300 and 3000 mg $L^{-1}$) and high grade if the dipstick showed a value of 3+ or 4+(level>3000 mg $L^{-1}$).

**Statistical analysis:** Statistical analysis was done using the software of the Statistical Programme for Social Sciences (SPSS) version 17. Descriptive characteristics of the group variables were expressed as mean values and standard deviation. Mean values between the two groups were compared using paired T test. A P-value of <0.05 was considered statistically significant (providing a 95% confidence interval).

## RESULTS

Out of 105 primigravidae with singleton pregnancy recruited before their 20th week of pregnancy, six did not attend ante natal clinic regularly and ten did not show up for delivery in the hospital for unknown reasons. Only 89 primmigravidae completed the study, out of which nine (10.1%) had pre-eclampsia. Also, three (3.4%) of the studied population had pregnancy induced hypertension only while 77 (86.5%) remained normotensive. Paedal oedema was found to be mild in all the preeclampsia cases.

There was no significant difference (p>0.05) in booking systolic and diastolic blood pressures but there was a significant difference (p<0.05) in systolic and diastolic blood pressures among the preeclamptic patients and the controls. Also, the outcome of the pregnancy shows that two patients had abortion, one had preterm delivery and one had intrapartum eclampsia.

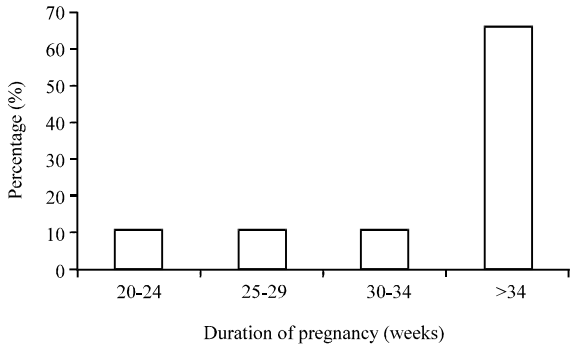


Fig. 1: Percentage distribution of preeclampsia amongst weeks of pregnancy

Table 1: Average systolic and diastolic blood pressure amongst preeclamptic patients

| Duration of pregnancy (weeks) | N | Systolic BP (mmHg) | Diastolic BP (mmHg) |
|---|---|---|---|
| 20-24 | 1 | 150 | 100 |
| 25-29 | 1 | 150 | 100 |
| 30-34 | 1 | 160 | 110 |
| >34 | 6 | 163 | 107 |

Figure 1 shows the percentage distribution of preeclampsia amongst the duration of pregnancy. Most cases of preeclampsia (66%) were observed at above 34 weeks duration while it was observed in only 11% cases at 20-24, 25-29 and 30-34 weeks pregnancy duration.

Figure 1 shows that 66% of preeclamptic patients had preeclampsia at>34 weeks, while 11% had preeclampsia at 20-24, 25-29 and 30-34 weeks, respectively.

Table 1 shows the average systolic and diastolic blood pressure amongst the preeclamptic patients. It followed the same pattern as distribution of preeclampsia amongst duration of pregnancy. The mean systolic and diastolic blood pressures with corresponding duration of pregnancy (in weeks) as observed were shown. The highest average systolic blood pressure of 163 mmHg was observed at>34 weeks pregnancy while the highest average diastolic blood pressure of 110 mmHg was observed at 30-34 weeks range.

Table 2 shows serum total protein, albumin, globulin and creatinine levels and aspartate transaminase activity; systolic and diastolic blood pressures amongst preeclamptic patient and the controls. While there was a significant decrease (p<0.05) in serum total protein, albumin and globulin of the preeclamptic patients

Table 2: Serum total protein, albumin, globulin and creatinine levels and aspartate transaminase activity amongst preeclamptic patient and the controls

| | Preeclamptic patient | Control | T-value | p-value |
|---|---|---|---|---|
| Total protein (g $L^{-1}$) | 50.11±3.33 | 69.33±1.50 | 19.80 | 0.00* |
| Albumin (g $L^{-1}$) | 22.67±1.22 | 37.78±2.59 | 22.40 | 0.00* |
| Globulin (g $L^{-1}$) | 27.44±3.78 | 31.56±3.25 | 3.12 | 0.01* |
| Creatinine (μ mmo $L^{-1}$) | 90.44±1.74 | 62.67±1.58 | 36.60 | 0.00* |
| Aspartate transaminase (U $L^{-1}$) | 27.11±4.73 | 8.56±3.17 | 14.40 | 0.00* |
| Systolic blood pressure (mmHg) | 160.00±11.1 | 113.00±7.07 | 11.40 | 0.00* |
| Diastolic blood pressure (mmHg) | 104.00±5.27 | 72.20±6.67 | 14.50 | 0.00* |

Values are presented as Mean±SD, SD: Standard deviation, values in a row and column are significantly different at $p<0.05$ level

(50.11±3.33, 22.67±1.22 and 27.44±3.78, respectively) compared to the control (69.33±1.5, 37.78±2.59 and 31.56±3.25, respectively), there was a significant increase ($p<0.05$) in serum creatinine levels and aspartate transaminase activity in the preeclamptic patients (90.44±1.74 and 27.11±4.73, respectively) compared to the controls (62.67±1.58 and 8.56±3.17, respectively).

Table 1 above shows the mean systolic and diastolic blood pressure and the duration of pregnancy at diagnosis of preeclampsia. The highest mean systolic blood pressure of 163 mmHg was observed at>34 weeks pregnancy while the highest average diastolic blood pressure of 110 mmHg was observed at 30-34 weeks range.

## DISCUSSION

Proteins are normally prevented from passing into urine by both the glomeruli (which provide a barrier that keeps larger plasma proteins inside the blood vessels) and the tubules (which almost totally reabsorb small proteins that do get through the basement membrane). In non-pregnant women total protein excretion greater than 150 mg daily is abnormal.

In normal pregnancy, an increase urinary protein excretion is observed due to a combination of increased glomerular filtration rate and increased permeability of the glomerular basement membrane (Roberts *et al*., 1996). Thus, a total protein excretion exceeding 300 mg/24 h in pregnant women is considered abnormal (Higby *et al*., 1994).

Proteins obtainable from the urine could be either of glomerular (albumin and proteins with Mw>67,000) or tubular origin (proteins with Mw<67,000). The quantity of protein that is excreted in the urine varies widely. Significant proteinuria in pregnancy is defined as ≥300 mg in a 24-h urine collection or 1+ or greater on urine dipstick testing of two random urine samples that are collected at least 4 h apart (Brown *et al*., 2001).

Urine from preeclamptic patient generally demonstrates poor selectivity and there is no significant difference found to exist between this and other forms of primary renal disease (Simanowitz and MacGregor, 1974). Glomerular proteins of intermediate size, such as albumin, have been identified alone or in combination with varying concentrations of tubular proteins (such as $\beta_2$-microglobulin) reflecting the tubular damage that can occur in severe preeclampsia (Winkler *et al*., 1988; Quaas *et al*., 1987). About 40% of urinary proteins are glomerular in origin while proteinuria of tubular origin constitutes about 60% (mostly Tamm-Horsfall protein) (Conrad *et al*., 2009).

Quantitatively, the range amount of protein obtainable in the urine of a preeclamptic patient is 300-600 mg/24 h. In the eclamptic patients, increased amount of mixed protein, comprising of both lower and higher molecular weight than albumin, corresponding to mixed glomerular and tubular proteinuria pattern was obtained. Quantitatively, these proteins range between 1200 to 4600 mg/24 h.

Hypertension, another important sign in preeclampsia, result from abnormal vasoconstriction and this is due to derangement of endothelial-derived vasoactive factors which is thought to result in the predominance of vasoconstrictors (endothelin and thromboxane A2) over vasodilators (Nitric oxide and prostacyclin) (Hladunewich *et al*., 2007).

Hypertension was found to complicate 10.1% (9 out of 89) of pregnancies in this study. This is in agreement with the earlier finding of Lopez-Jaramillo *et al*. (2001) who reported that hypertensive disorders affect 5-10% of all pregnancies.

Also from this study, serum total protein and albumin levels were found to be significantly low ($p<0.05$) in PE as compared to the control. PE is associated with increased capillary permeability secondary to endothelial damage and this seems to be partly responsible for the observed proteinuria and consequent significantly low serum total protein and albumin levels. These findings corroborate the earlier work of Bhatia *et al*. (1987). Hypoalbuminemia in preeclampsia is thus a consequent of urinary protein loss and reduced hepatic blood flow secondary to haemoconcentration created by higher filtration pressure in the capillaries.

Also, serum AST and creatinine levels were found to be significantly elevated ($p<0.05$) in PE. Similar result had been reported by Benoit and Rey (2011). The elevated serum transaminase levels in PE may be due to arteriolar spasm that occurs which involves the myocardium, liver,

kidney and brain. The arteriolar constriction in these tissues usually results in tissue hypoxia and resultant damage to the hepatocellular integrity and thus release of AST into the plasma. The confirmation of hepatic disorder as a cause of increased AST activities in PE could be made by the determination of serum Alanine Transaminase (ALT) activities which is more liver specific than AST.

Electrophoretic proteinuria pattern in pregnancy could be of diagnostic importance for early detection of preeclampsia and eclampsia in pregnant women with clinical features suggestive of preeclampsia and eclampsia before the development of classical preeclamptic and eclamptic features.

## CONCLUSION

Though, the known definitive treatment of preeclampsia is delivery of the baby, the degree of proteinuria, gestational age, maternal and fetal clinical condition, available facilities and expertise at the managing centre and available laboratory results of hematologic and biochemical parameters should be considered for the timing delivery of women with pre-eclampsia. In the absence of renal disease, liver disease, muscular disease, pancreatitis and myocardial infarction; high levels of AST, blood pressure greater than or equal to 140/90 mmHg and proteinuria of ≥300 mg/24 h may be indicative of PE.

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