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# Some Patterns of Haemostatic Parameters Among Pregnant Women with Hypertensive Disorders in Owerri, Imo State, Nigeria

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**Abstract**

*Hemostatic parameters of pregnant women with hypertensive disorders in owerri were studied using standard methods. The parameters include PT, APTT, Fibrinogen, t-PA, D-dimer. A total of 200 pregnant women between ages of 18 and 45 years of age were recruited for the study. They consisted of 50 normotensive pregnant women as the control group and 150 hypertensive as the test subjects. The test group was further divided into 3 viz; 50 chronic hypertensive, 50 gestational and 50 preeclamptic pregnant women as group as groups 1, 2 and 3 respectively. The mean PT(secs.) values were 11.69±1.02, 11.98±0.94, 12.79±0.78 and 13.86±1.4 respectively, in control, groups 1, 2 and 3. The APTT(secs) mean values in control, groups 1, 2 and 3 were 28.59±2.33, 29.43±2.67, 30.20±2.73 and 31.52 respectively. The mean values obtained for D-dimer (ng/ml) were 191.72±41.92, 207.30±60.71, 249.52±62.08 and 268±59.51 in control, groups 1, 2 and 3 respectively. In control, fibrinogen (mg/ml) mean value obtained was 521.74±118.02, where as in the test groups, 532.97±111.40, 602.52±103.80 and 671.98±97.37 were respectively obtained in groups1, 2 and 3. The mean respective values of t-PA (ng/ml) in control, group 1, 2 and 3 were 2.43±0.55, 2.49±0.49, 2.84±0.54 and 2.90±0.57. All the haemostatic parameters: PT, APTT, Fibrinogen, D- dimer and t-PA values increased across the test groups when compared with the control groups and they were found to be statistically significant (P=0.0001). From this study, haemostatic parameters increased in the test subjects indicating inflammatory activities in hypertensive disorders of pregnancy.*

## Introduction

A range of illnesses that are linked with high blood pressure during pregnancy is referred to as hypertensive disorders of pregnancy, or HDP for short. Another name for this condition category is maternal hypertensive disorder. It is a catch-all word that refers to preexisting (chronic) hypertension, hypertension that develops during pregnancy, and preeclampsia. It is estimated that between 5 and 10 percent of all pregnancies are affected by complications, making it a major source of maternal and perinatal morbidity and death across the globe (Braunthal & Brateanu, 2019). It has been estimated that the prevalence of hypertensive

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disorder in pregnancy, also known as HDP, ranges from 5 to 17 percent in Nigeria (Singh et al., 2014).

A blood pressure reading that is more than 140/90 mmHg on at least two separate occasions and at least six hours apart is considered to be hypertensive. In the context of pregnancy, hypertension is defined as having a systolic blood pressure that is at least 140 mm Hg or a diastolic blood pressure that is at least 90 mm Hg or above (140/90 mm Hg). The term "chronic hypertension" refers to an increase in blood pressure that occurred either before pregnancy, early in pregnancy (before 20 weeks), or does not decrease by the 12-week postpartum (AlSheeha et al., 2016; Robert et al., 2015). The new onset of hypertension (typically systolic BP > 140 mmHg and/or diastolic BP > 90 mmHg) after 20 weeks of gestation or occurring in the second half of pregnancy is referred to as gestational hypertension. This condition was formerly known as pregnancy induced hypertension (PIH) or transient hypertension. Preeclampsia is widely defined as the development of hypertension and substantial proteinuria after 20 weeks of gestation in women who would otherwise be considered to have normal blood pressure (Robert et al., 2015). It is the combination of high blood pressure during pregnancy and a recent onset of proteinuria (Rhaghupathy et al., 2012) accompanied by significant rates of maternal morbidity and death as well as uterine fetal growth limitation (Elosha et al., 2012).

It is possible for preeclampsia to develop from any of the hypertensive disorders. Up to 35 percent of women who have prenatal hypertension and up to 25 percent of those who have chronic hypertension are affected by this condition. However, it is assumed to be connected to a process of decreased placental perfusion that occurs during systemic vascular endothelial failure (Grande et al., 2014). The underlying pathophysiology that supports this shift is not fully known. HDP risk factors include a history of pre-eclampsia or hypertension in pregnancy, chronic kidney disease, hypertension, multifetal gestations, obesity, diabetes mellitus, autoimmune diseases like systemic lupus erythematosus, maternal age of >40 years at first pregnancy or >10year interval from last pregnancy, increasing BMI, multiple pregnancies, smoking, socioeconomic level, and African American race (Mulvany, 2012). HDP is more common in women of African American

The control of blood loss from a blood vessel that has been injured, as well as the dissolving of an excessive blood clot in situations of thromboembolism, are both aspects of hemostasis. During a normal human pregnancy, profound alterations in coagulation and fibrinolytic systems result in a hypercoagulable condition. This is a physiological adaptation that helps avoid significant bleeding during and after placental separation (Luis et al., 2003). According to Rupakala et al, (2018) it is thought that changes in the blood's ability to coagulate and fibrinolyze play a crucial part in the pathophysiology of preeclampsia. In preeclampsia, abnormalities of coagulation parameters such as prothrombin time (PT), activated partial thromboplastin time (APTT), and fibrinogen levels are typically observed, even in the presence of normal platelet count (Leduc et al., 2011). These abnormalities can be seen in the prothrombin time (PT), activated partial thromboplastin time (APTT), and fibrinogen levels. According to Jahromi (Jahromi & Rafiee, 2009), the measurement of APTT seems to be significant for the early diagnosis of coagulation problems in patients with preeclampsia who have normal platelet counts. This is the case even though the patients have normal platelet counts. In a similar manner, preeclampsia is linked to fibrin accumulation in the microvasculature (Pinheiro et al., 2013) and endothelial dysfunction (Luis et al., 2003). Both D-dimer and tissue plasminogen activator (t-PA) have been used as a marker to assess the generation and breakdown of fibrin in vivo. D-dimer has also been used to evaluate endothelial dysfunction. When compared to pregnant patients with normotension, those who have preeclampsia had higher levels of D-dimer and t-PA antigen, according to the findings of a number of investigations (Bremme, 2003).

Since HDP is a highly complex syndrome with multiple genetic, nutritional, and other environmental factors as well as population factors that intervene on the parameters under study (Mtali et al., 2019), it would not be justifiable to generalize their findings down to our setting and apply them there. However, the majority of previous studies focused mostly on preeclampsia. As a result, this research will be conducted in order to give accurate and pertinent data that might be used to forecast the development, monitoring, and prognosis of HDP in the study region.

HDP is still a serious public health problem in both developed and developing nations, and it is a factor that contributes to maternal and perinatal morbidity and death across the world. The complication has been a burden on the globe and is characterized by the presence of cardiovascular disease, renal illness, hemorrhagic disorder, and multisystem problem. Because of this, the only way to minimize mortality is by the early discovery of the symptoms, diligent monitoring, and treatment of the condition. However, the majority of the studies were conducted mostly on preeclampsia and outside of the research region. As a result, it is possible that the results cannot be generalized to all women in Nigeria. Therefore, the purpose of this research was to give data on the level of several haemostatic indicators among pregnant women who had HDP in Owerri, which is located in the south-eastern region of Nigeria. having knowledge of the impacts that the condition has, as well as the correlations it has with the parameters that are being studied. It is possible that this will give a suitable foundation as part of the diagnosis and care of women in this region who have HDP, hence decreasing the risk of problems.

## Methods

### The Study Area

The Federal Medical Centre Owerri, located in Imo State, Nigeria, was the site of this research project. One of the 36 states that make up Nigeria is called Imo state. It may be found in Nigeria's South Eastern Zone, between the latitudes of 4045'N and 7015'N, and between the longitudes of 6050'E and 7025'E. Owerri, Orlu, and Okigwe are the three senatorial zones that make up Imo State. Okigwe is the capital of the state. Igbo is the native people that live in the area that is now known as Owerri, which is the capital of Imo State. Owerri Municipal, Owerri North, and Owerri West make up its constituent parts. The location's geographical coordinates are 5.48 degrees North latitude and 7.03 degrees East longitude. The population is made up of people working in a wide variety of professions, such as merchants, farmers, craftsmen, public and civil employees, politicians, students, and so on. Owerri, the capital city of Imo State, is home to the Federal Medical Centre, which is a tertiary hospital. This hospital is a tertiary referral center that offers sufficient medical treatment to ill people in general as well as pregnant women. The Gyneocology and Obstetrics section of the hospital has a total of 81 available bed spaces for patients. Other collecting centers may be found in Owerri, in the state of Imo. These include the Vaden specialty clinic and maternity as well as the Primary health facility Umuguma.

### Study Population

The study included a total of 200 pregnant women, ranging in age from 18 to 45 years old; 150 hypertensive pregnant women and 50 normotensive pregnant women, all of whom were in their third trimester (28-40 weeks) and attended the antenatal clinic at the Federal medical Centre Owerri, were recruited for the study. Based on the findings of Chang et al. (2013), the prevalence rate was determined to be 11 percent. The size of the sample was determined by using the formula developed by Guzik & Touyz (2017).

### Experimental Design

The participants in this research were separated into two groups: those with hypertension disorders in pregnancy (150 total subjects), who acted as the test group, and normotensive pregnant women (100 total patients), who acted as the control group (50 subjects). After that, the test group was split up into the following three groups: Group 1 – 50 Women who are pregnant and have gestational hypertension have a systolic blood pressure that is higher than 140 mm Hg and a diastolic blood pressure that is higher than 90 mm Hg and it begins after the 20th week of pregnancy. Group 2 - 50 Chronically hypertensive pregnant women: systolic blood pressure more than 140 mm Hg and diastolic blood pressure greater than 90 mm Hg occurring before the 20th week of gestation and continuing after delivery. Pre-eclamptic women are classified as being in Group 3 if they have a systolic blood pressure that is higher than 140 mm Hg and a diastolic blood pressure that is higher than 90 mm Hg, and they also have proteinuria that is up to 1+.

### Sample Collection and Preparation

In order to evaluate the patient's hemostatic characteristics, a sample of venous blood measuring four milliliters (4 ml) was taken from the ante cubital vein in the lower arm. A haemostatic test requires 2.0 milliliters to be placed into 0.25 milliliters of an anticoagulant solution containing 3.2% trisodium citrate. In order to extract the plasma from the sample that was contained inside the citrate anticoagulated test tube, it was centrifuged for five minutes at a speed of three thousand revolutions per minute. After allowing the sample to clot at room temperature in the simple test tube, it was then centrifuged to separate the serum from the other components of the sample. Immediately after the samples were collected, coagulation parameters were determined based on the analysis of the samples.

### Laboratory Procedures

Prothrombin Time Estimation (PT), Activated Partial Thromboplastin Time Estimation (APTT), Fibrinogen Assay, D-dimers and Tissue Plasminogen Activator (t-PA) were determined with Commercial ELISA Kit by Melsin Medical Co., Limited (Guzik & Touyz, 2017).

### Statistical Analysis

The Statistical Package for the Social Sciences was used for all of the statistical analyses that was done (SPSS version 21). The numbers were reported in the form of a percentage and the mean together with the standard deviation, and the findings were tabulated and charted. For the purpose of analyzing the differences between the two groups, an analysis of variance (ANOVA) and a student's t-test were used. The Chi-square test ($\chi 2$) was used to make comparisons between categorical variables. The significance level was determined to be p 0.05. Pearson's correlation was used in order to do the analysis of the connection.

## Results and Discussion

Table 1. Mean ± standard deviation values of coagulation and fibrinolytic parameters in hypertensive pregnant women and normotensive pregnant women.

| PARAMETERS | CONTROL (n=50) | TEST (n=150) | T-test | P-value |
|---|---|---|---|---|
| PT (seconds) | 11.69 ± 1.02 | 12.88 ±1.33* | 5.794 | 0.0001 |
| APTT (seconds) | 28.59 ± 2.33 | 30.72 ±2.98* | 4.597 | 0.0001 |
| Fibrinogen (mg/dl) | 521.74 ± 118.02 | 602.32 ± 118.26* | 4.173 | 0.0001 |
| D-dimer (ng/ml) | 191.72 ±41.92 | 241.63 ± 66.54* | 5.047 | 0.0001 |
| t-PA (ng/ml) | 2.43 ±0.55 | 2.74± 0.56* | 3.450 | 0.001 |

Key: PT = Prithrombin Time
APTT = Activated Partial Thromboplstin Time
t-PA = Tissue Plasminogen Activator
n = Sample Size
* = Statistically Significant When Compared to Control

The mean prothrombin time was higher in test (12.88 ±1.33 seconds) than control (11.69 ± 1.02 seconds), and the difference was significant ($p<0.05$). Activated partial thromboplastin time was found to be 30.72 ±2.98 seconds for the Test group and 28.59± 2.33 second for the control group. The difference was statistical significant ($p<0.05$) between the two groups. The mean fibrinogen was higher in test (602.32 ± 118.26 mg/dl) than control (521.74 ± 118.02 mg/dl), and the difference was significant ($p<0.05$). D-dimer and tissue plasminogen activator of study group (241.63 ± 66.54 and 2.74± 0.56 ng/ml) was higher than the control (191.72 ±41.92 and 2.43 ±0.55 ng/ml) respectively; and their difference is significant ($p<0.05$).

Table 2. Mean ± Standard deviation values of coagulation and fibrinolytic parameters in control and various study groups.

| PARAMETER | CONTROL (n=50) | GROUP 1 (n=50) | GROUP 2 (n=50) | GROUP 3 (n=50) | F-value | P-value |
|---|---|---|---|---|---|---|
| PT (seconds) | 11.69 ± 1.02 | 11.98 ±0.94 | 12.79 ±0.78* | 13.86 ±1.43* | 41.560 | 0.0001 |
| APTT (seconds) | 28.59 ± 2.33 | 29.43 ±2.67 | 30.20 ±2.73 | 31.52 ±3.12* | 13.260 | 0.0001 |
| Fibrinogen (mg/dl) | 521.74 ± 118.02 | 532.97 ± 111.40 | 602.00 ± 103.80* | 671.98 ± 97.37*[b] | 20.791 | 0.0001 |
| D-dimer (ng/ml) | 191.72 ±41.92 | 207.30 ± 60.71 | 249.52 ± 62.08* | 268.08 ±59.51*[b] | 19.779 | 0.0001 |
| t-PA (ng/ml) | 2.43 ±0.55 | 2.49± 0.49 | 2.84± 0.54*[b] | 2.90± 0.57*[b] | 9.844 | 0.0001 |

Key: PT = Prithrombin Time
APTT = Activated Partial Thromboplstin Time
t-PA = Tissue Plasminogen Activator
n = Sample Size
* = Statistically Significant When Compared to Control
A = Statistically Significant different ($p<0.05$) compared to group1.

One-way analysis of variance shows a significant increase ($p=0.001$) in PT of study groups across the group with group 3 women with the highest PT of (13.86±1.43 seconds) and control with the least age (11.69 ± 1.02 seconds). Post hoc in between comparism shows a significant ($p>0.05$) increase in PT of group3 (13.86± 1.43 seconds) compare to the group 1 (11.98 ±0.94).

APTT of control, group 1, group 2 and group 3 were 28.59 ±2.33, 29.43 ±2.67, 31.20± 2.73 and 31.52 ±3.12 seconds respectively, they were significantly ($p=0.001$) increased across the group. Fibrinogen was significantly ($P=0.0001$) increased across the group with normotensive (521.74 ±118.02 mg/dl), group 1 (532.97 ±111.40mg/dl), group 2 (602.00± 103.80mg/dl) and group 3 (671.98 ±97.37mg/dl). In between comparism showed a statistical significant increase in the group 3 and 2 compared to group 1 ($p<0.05$).

D-dimer was increased across the group and their difference was significant ($p=0.0001$). Group 1 (207.30± 60.71ng/ml), group 2 (249.52± 62.08ng/ml) and group 3 (268.08 ±59.51ng/ml) were statistically significant ($p<0.05$) decreased when compared to the control (191.72± 41.91ng/ml). Group 2 and 3 was statistically significantly higher compared to group 1. Tissue plasminogen activator was increased across the group and their difference was significant ($p=0.001$). Group 2 (2.84±0.54ng/ml) and group 3 (2.90±0.57ng/ml) were statistically

significantly ($p<0.05$) decreased when compared to the control (2.43± 0.55ng/ml); while Group 1 (2.49± 0.47ng/ml) was non significantly ($p>0.05$) higher compared with the control.

There were a total of 200 pregnant women participated in this trial, including 150 individuals with HDP and 50 normotensive controls. In this research, hypertensive pregnant women had a longer prothrombin time than normotensive pregnant women. This rise was more pronounced in preeclamptic women than in those with chronic or gestational pregnancy. APTT was considerably lengthened in hypertensive pregnant women compared to normotensive pregnant women, according to the research.

In the research done by Halder and Barui (2020), prothrombin time and activated partial thromboplastin time were shown to be extended in severely hypertensive pregnant women, particularly in preeclamptic patients. The findings supported this research. Also, in the research done by Sharma et al., 2016), there was a statistically significant correlation between PIH severity and an increase in APTT. This was consistent with this research.

Joshi et al. (2015) did a research in which they discovered that pre-eclampsia and eclampsia are characterized by thrombocytopenia and coagulation abnormalities, namely APTT prolongation. The lengthening of the prothrombin time shows the usage of clotting factors caused by mild intravascular coagulation. Jambhulkar et al. (2011) found that the mean APTT in patients with severe PIH was considerably increased. In severe PIH, a significant extension of the PTT shows consumption of coagulation factors, particularly factor VIII.

The test participants had higher fibrinogen levels than the control subjects. Pregnancy is a hypercoagulable condition owing to increased synthesis of all coagulation factors, including fibrinogen, factors VIII, IX, and X, and a considerable decrease in the fibrinolytic pathway due to increased synthesis of plasminogen activator inhibitors types 1 and 2. In pregnancy-induced hypertension and preeclampsia, the alterations in the coagulation and fibrinolytic system are more prominent. Our research was consistent with those of (Olayiwola et al., 2018).

D-dimer is elevated in hypertensive disorders of pregnancy due to a compensated state of low-grade intravascular coagulation; moreover, this elevation indicates that the fibrinolytic system remains functionally active despite a substantial decrease in fibrinolytic capability. In this research, the readings of pre-eclamptic hypertensive pregnant women were considerably greater than those of their control counterparts, suggesting enhanced intravascular coagulation and activation of fibrinolysis. This parallels the results of several scholars (Abbas et al., 2012).

Tissue plasminogen activator (t-PA) levels were higher in hypertensive women than in healthy controls. It is recognized that endothelial cell (EC) dysfunction is involved with the development of pre-eclampsia. This is more likely to enhance the expression of endothelial-derived fibrinolytic proteins, their inhibitor, and their products in pre-eclamptic patients than in normotensive pregnant women. This is confirmed by the current study's result that plasma concentrations of endothelially produced t-PA and PAI-1 were considerably greater in patients than in controls. This resembles the research conducted by (Teng et al., 2019).

The hypertensive disease of pregnancy is a phenomenon unique to pregnancy characterized by reduced organ perfusion owing to vasospasm and endothelial activation (Robert et al., 2015). Roberts and colleagues hypothesized that changes in endothelial cell activity caused by activating substances released by the placenta begin the pre-eclamptic clinical symptoms. In addition, unknown substances, possibly from the placenta, are released into the maternal circulation and cause activation and malfunction of the endothelium of the blood vessels (Perry, 1994). Therefore, endothelial cell damage plays a crucial role in pre-eclampsia and may be responsible for the observed hemostatic alterations in this disease. Endothelial-derived factors such as t-PA may serve as indicators of endothelial activity in hypertensive disorders of pregnancy (Ducloy, 2020). HDP is thus characterized by a hypercoagulable condition in the

mother, intravascular coagulation, microthrombosis in several organs, and impaired uteroplacental circulation.

D-dimer and tPA were favorably linked with prothrombin time and fibrinogen. This demonstrates the linear connection between coagulation and fibrinolysis. The hypertensive condition of pregnancy is marked by hypercoagulability and intravascular coagulation in the mother. Hypertension during pregnancy results in endothelial cell dysfunction, which increases the production of endothelium-derived fibrinolytic proteins such as tissue plasminogen activator. This results in an increase in the synthesis of all coagulation components, particularly fibrinogen, which leads to tissue clotting, followed by the breakdown of fibrin and the generation of D-dimers.

## Conclusion

We may infer from our work that hypertensive disorders of pregnancy are associated with considerable alterations in hemostatic measures. Coagulation and fibrinolytic factors rise in hypertensive disorders of pregnancy, according to the emerging picture. Thus, we may infer that the coagulation profile is a valid indication of hypertensive disease of pregnancy, thus reducing morbidity and death.

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