



## Effects of Gravity on Atherogenic Indices in Normotensive and Hypertensive Second Trimester Pregnant Women

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### Authors' contributions

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### ABSTRACT

**Background:** Pregnancy results in certain physiological and metabolic changes that results to shift in certain biochemical markers and could even result in hypertension in some women thus predisposing them to risk of cardiovascular disease. While this is true, some women express these predisposing risk factors in subsequent pregnancies. Therefore, it may be a significant contribution to understand the dynamics of artherogenic indices with increasing number of pregnancies.

**Aim:** The goal of the study was aimed to assess gravity effect on artherogenic indices in both normotensive and hypertensive second-trimester pregnant women.

**Materials and Methods:** At Rivers State University Teaching Hospital, a cross-sectional study was carried out with 100 pregnant women. The consenting patients who met the inclusion criteria were classified into two groups: normotensive (50 normotensive pregnant women in their second trimester) and hypertensive (50 hypertensive pregnant women in their second trimester) (HPW2T). The participants were subsequently split into three subgroups depending on gravity: primigravida (no of pregnancy=1), multigravida (no of pregnancies>1), and grand multigravida (no of pregnancies≥5). For the assessment of TC, TG, HDL, and LDL, fasting blood samples were taken using the venepuncture technique. Mathematically, artheriogenic indices (AIP, CR-I, CR-II, AC, and APoB/APoA1) were calculated. At a P-value>0.05, the data was examined using ANOVA and the Tukey comparison test.

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**Results:** There was no significant difference in arteriogenic indices between the gravidity groups in the normotensive group, with a P-value>0.05, which was also the cases among those in the hypertensive group.

**Conclusion:** The study has shown that gravidity does not have any effect on arteriogenic indices among normotensive and hypertensive pregnant women in the second trimester in Rivers State University Teaching Hospital.

*Keywords: Normotensive; hypertensive; arteriogenic; pregnancy; second trimester.*

## 1. INTRODUCTION

Hypertension also called high blood pressure or arterial blood pressure is a persistent medical state whereby there is an increase in the pressure of blood in the arteries. Blood pressure levels are usually  $\geq 140/90$  mm/Hg prior to pregnancy or sooner than the 20<sup>th</sup> week of gestation. Over the years, it has been considered a major risk factor associated with disease of the cardiovascular system [1]. Pregnancy-related hypertensive disorders, such as pregnancy-induced hypertension (PIH) and preeclampsia, are among the main causes of maternal and newborn morbidity globally [2]. In the industrialized world, preeclampsia affects 2-4 percent of pregnancies and is a primary cause of maternal and newborn morbidity and mortality [3].

The period during which a fetus develops inside a woman's womb or uterus is referred to as pregnancy. From the last menstrual period to delivery, it normally lasts about 40 weeks, or slightly over 9 months. Trimesters are the terms used by doctors to describe the three stages of pregnancy. The three trimesters of a normal pregnancy are determined by the gestational age, which is measured in weeks and months. The first trimester lasts from conception through the 12th week of pregnancy (2 months and 3 weeks). The second trimester lasts 13-27 weeks (3 months to 6 months and 2 weeks), whereas the third trimester begins at 28 weeks and ends until the baby is born (7 months to 9 months) [4]. The amount of times a woman has been pregnant is referred to as gravidity [4].

Preeclampsia and pregnancy-induced hypertension affect roughly 7% of all pregnancies, and severe preeclampsia is a leading cause of severe maternal morbidity, including stroke and liver rupture [5]. Preeclampsia is a condition that occurs after 20 weeks of pregnancy and is characterized by chronic or gestational hypertension as well

as proteinuria due to a faulty placentation [6]; eliciting perfun and ischaemia in the uteroplacental blood [7]. Preeclampsia has no established etiology, but it is suspected to be caused by an implantation problem [8].

Several attempts have been undertaken to find novel or emergent cardiovascular risk factors in order to enhance the prediction of cardiovascular disease. Several lipoprotein ratios or "atherogenic indices" have been created in an attempt to improve the predictive power of the lipid profile [9]. These indices may show to be a more effective alternative to standard studies. One of these is the Cardiac Risk Ratio (CRR), which is derived from the total cholesterol to High Density Lipoprotein cholesterol (HDL) ratio and is often used for risk assessment of cardiovascular disease (CVD) [10]. The Atherogenic Index of Plasma (AIP), which is computed as  $\log(\text{Triglyceride (TG)/High Density Lipoprotein-Cholesterol})$ , is another index. Because it is elevated in persons at higher risk for coronary heart disease and is inversely connected with Low Density Lipoprotein particle size, it has lately been recommended as a marker of plasma arteriogenicity [9]. The balance between risk and protective lipoprotein factors is theoretically reflected by the connection of TGs and HDL-C in this simple ratio, and both TGs and HDL-C are widely measured and available [11]. Another statistic is the Artheriogenic Coefficient (AC), which is determined by the ratio of non-HDL cholesterol to HDL cholesterol. Non HDL-c is simply calculated without the requirement for the patient to fast beforehand. It's basically the cholesterol equivalent of an apo B level, with a greater correlation coefficient than LDL cholesterol concentration [12]. Many research have looked at the effects of gravidity on arteriogenic indices in normotensive and hypertension second-trimester pregnant women, but this one focuses on the effects of gravidity on arteriogenic indices in normotensive and hypertensive second-trimester pregnant women.

## 2. MATERIALS AND METHODS

### 2.1 Study Design

A total of one hundred pregnant women participated in the cross-sectional study. Based on the clinical history in their clinical folder, fifty of the participants were normotensive and the other fifty were hypertensive. Both groups (hypertensive and normotensive) had three sub-groups depending on gravidity (number of pregnancies): primigravida (number of pregnancies=1), multigravida (number of pregnancies>1), and grand multigravida (number of pregnancies≥5). The primigravida subgroup contained fifteen participants, the multigravida group had twenty seven participants, and the grand multigravida group comprised eight participants in the normotensive group. The primigravida subgroup comprised twenty one participants, the multigravida group had twenty five participants, and the grand multigravida group contained four participants in the hypertensive group. In Rivers State University Teaching Hospital, their artheriogenic characteristics were tested individually to see if gravidity had an effect on artheriogenic indices in 2nd trimester pregnant women.

### 2.2 Study Area

The research was conducted at the Rivers State University Teaching Hospital (previously known as Braithwaite Memorial Specialist Hospital) in Port Harcourt, Nigeria's capital city.

### 2.3 Study Population

The target group is pregnant women in their second trimester, who are further separated into two groups: normotensive second trimester pregnant women and hypertensive second trimester pregnant women.

### 2.5 Eligibility Criteria

This study included all apparently healthy pregnant women and hypertensive pregnant women, including those on medication, who were attending prenatal care for the first time during their current pregnancy. Exclusion criteria included a recent history of blood transfusion, surgery, or inability to offer informed permission.

### 2.6 Selection Method

Participants who have met the inclusion criteria and provided consent for study participation were

selected through simple random technique using a numbering system described by some researchers in a study on pregnant women [13,14].

### 2.7 Sample Collection Method

Total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), and low density lipoprotein (LDL) were measured in fasting blood samples taken by venepuncture (LDL). Blood was carefully emptied into plain vacutainer tubes, allowed to clot, then centrifuged for 10 minutes at 1500rpm. The serum was separated and kept at -4°C until it was time to conduct the analysis [15,16].

### 2.8 Laboratory Methods

#### 2.8.1 Total Cholesterol serum determination

The total cholesterol was quantified using an enzymatic technique [17].

#### 2.8.2 Principle

After enzymatic hydrolysis and oxidation, the cholesterol is measured. In the presence of phenol and peroxidase, the indicator quinoneimine is produced from hydrogen peroxide and 4-aminoantipyrine. The quantity of color produced is proportional to the amount of cholesterol present in the blood.

#### 2.8.3 Procedure

The assay circumstances were taken into account. With distilled water, the instrument was zeroed. One milliliter of cholesterol reagent was pipetted into clean dry test tubes labeled blank, standard, and tests, with 10 milliliters of distilled water, standard, and sample added to their corresponding tubes. It was thoroughly mixed by tilting the bottoms of the tubes and incubated for 5 minutes in a water bath at 37°C. In a spectrophotometer, the absorbance of the standard and test samples was measured against the blank at 540nm wavelength.

#### 2.8.4 Determination of high-density lipoprotein (HDL) cholesterol in serum

HDL-C was quantified using an enzymatic technique [18]

#### 2.8.5 Principle

The addition of phosphotungstic acid in the presence of magnesium ions quantitatively

precipitates low density lipoprotein (LDL and VLDL) and chylomicron fractions. The cholesterol concentration in the HDL fraction that remains in the supernatant is measured using an enzymatic technique after centrifugation.

### 2.8.6 Procedure

The blood samples were placed in tubes and centrifuged at 12,000 rpm for five minutes. The supernatant (sera) was separated and organized into control, standard, and sample tubes according to the labels. 200µl of precipitating reagent (R) and 20µl of sample were placed in test tubes, 20µl of standard in the standard tube, and distilled water in the blank tube. It was properly blended by tilting the bottoms of the tubes and let to stand at room temperature for 10 minutes. The contents of the tubes were centrifuged at 12,000 rpm for 2 minutes. After that, the clear supernatant was collected and HDL cholesterol was measured.

### 2.8.7 Determination of triglycerides in serum

The enzymatic approach is used to quantify triglycerides [19].

### 2.8.8 Principle

After enzymatic hydrolysis using lipases and oxidation, triglycerides are measured. Under the catalytic effect of peroxidase, a quinoneimine is produced from hydrogen peroxide, 4-aminophenazone, and 4-chlorophenol. The amount of color generated in the sample is related to the triglyceride concentration.

### 2.8.9 Procedure

The assay circumstances were taken into account. With distilled water, the instrument was zeroed. As a blank, standard, and test, 1ml of triglyceride reagent was applied to the tubes. The tubes were filled with 10µl of standard and sample, mixed, and incubated at 37°C for 5 minutes. The absorbance of samples was measured against a blank using a 1cm light path (cuvette) at a wavelength of 505 nm.

### 2.8.10 Determination of low-density cholesterol (LDL-C)

Friedewald's equation was used to compute LDL cholesterol [20].

$$\text{LDL - Cholesterol} = \text{Total Cholesterol} - (\text{TG}/2.2) - \text{HDL}$$

The atherogenic index and lipid ratios were calculated using the following established formulas:

AIP = Log (TG/ HDL-C): Reference Range = Low risk (-0.3 – 0.1), Moderate risk (0.1 – 0.24), High risk (>0.24) (World Health Organization (WHO), [21]

CRI-1 = TC/HDL-C: Reference Range = Low risk (< 1-3), Moderate risk (3-5), High risk (>5) [21].

CRI-II = LDL-C /HDL-C: Reference Range =Low risk (< 1-3), Moderate risk (3- 5), High risk (> 5) [21].

AC = TC – HDL-C/ HDL-C: (Reference >3.0) [21]

Apo B/ Apo A1: Reference range = (low risk 0.30, moderate risk 0.6 and high risk 0.8) [21].

## 2.9 Statistical Analysis

GraphPad Prism Version 8.0.2.263 was used to analyze the data from the study. The information was presented as a mean and standard deviation. One-way analysis of variance was used to compare the means (ANOVA). The Tukey comparison test was employed to ensure that there were significant differences between the groups. The result was considered significant at  $P < 0.05$ .

## 3. RESULTS

Tables 1.0 (a) and 1.0 (b) represents the effect of gravidity on atherogenic indices (AIP, CRI1, CRI2, AC and apo B/apo A1) in normotensive 2<sup>nd</sup> trimester pregnant women. There was no significant effect in gravidity on the indices in pregnant women with hypertension at 2<sup>nd</sup> trimester ( $p > 0.05$ ).

Tables 2.0 (a) and 2.0 (b) is a show the potency of gravidity on atherogenic indices (AIP, CRI1, CRI2, AC and apo B/apo A1) in hypertensive 2<sup>nd</sup> trimester pregnant women. In hypertensive pregnant women in the second trimester, gravidity had no significant effect on the indices ( $p > 0.05$ ).

## 4. DISCUSSION

The atherogenic index of plasma (AIP), castelli risk index (CRI 1), (CRI 2), Artherogenic Coefficient (AC), and ApoB/ApoA1 among pregnant women in Rivers State University and Rives State University Teaching Hospital were

**Table 1(a). Effect of gravidity on Atheriogenic indices in normotensives 2<sup>nd</sup> trimester**

Parameters	Normotensive women			P-value	F-value
	Primigravida (1) n = 15 (30%)	Multigravida(>1) n = 27 (54%)	Grand Multigravida (≥ 5) n = 8 (16%)		
AIP	0.18 ± 0.04	0.18 ± 0.06	0.20 ± 0.05	0.7611	0.2746
CRI 1	5.82 ± 0.82	5.19 ± 1.28	4.77 ± 0.78	0.0739	2.7550
CRI 2	4.16 ± 0.80	3.54 ± 1.21	3.07 ± 0.77	0.0521	3.1490
AC	4.82 ± 0.82	4.19 ± 1.28	3.77 ± 0.78	0.0739	2.7550
APoB/APoA1	0.36 ± 0.03	0.38 ± 0.05	0.36 ± 0.06	0.4512	0.8096

*P-value<0.05 is statistically significant*

**Table 1(b). The ANOVA Post – Hoc Findings Using Turkey Multiple Comparison Test for Effect of Gravidity on Atheriogenic Indices (Normotensive 2<sup>nd</sup> Trimester)**

Parameters	Primagravida Vs. Multigravida	Primagravida Vs. Grand multigravida	Multigravida Vs. Grand Multigravida
AIP	0.9783	0.8548	0.7405
CRI 1	0.1865	0.0836	0.6090
CRI 2	0.1650	0.0521	0.5203
AC	0.1865	0.0836	0.6096
APoB/APoA1	0.9475	0.4390	0.5233

*P-value<0.05 is statistically significant*

**Table 2(a). Effect of Gravidity on Atheriogenic Indices in Hypertensive 2<sup>nd</sup> Trimester**

Parameters	Hypertensive women			P-value	F-value
	Primigravida (1) n = 21(42%)	Multigravida(>1) n = 25 (50%)	Grand Multigravida (≥ 5) n = 4 (8%)		
AIP	0.22 ± 0.05	0.21 ± 0.07	0.18 ± 0.04	0.6246	0.4753
CRI 1	5.39 ± 0.98	5.33 ± 1.79	4.38 ± 0.25	0.4292	0.8612
CRI 2	3.64 ± 0.95	3.57 ± 1.58	2.79 ± 0.34	0.4115	0.9050
AC	4.39 ± 0.98	4.33 ± 1.79	3.38 ± 0.25	0.4292	0.8612
APoB/APoA1	0.34 ± 0.03	0.34 ± 0.03	0.35 ± 0.00	0.4629	0.7828

*P-value<0.05 is statistically significant*

**Table 2(b). The ANOVA Post – Hoc Findings Using Turkey Multiple Comparison Test for Effect of Gravidity on Atheriogenic Indices (Hypertensive 2<sup>nd</sup> Trimester)**

Parameters	Primagravida Vs. Multigravida	Primagravida Vs. Grand multigravida	Multigravida Vs. Grand Multigravida
AIP	0.8596	0.6181	0.7856
CRI 1	0.9914	0.4104	0.4399
CRI 2	0.9800	0.3865	0.4354
AC	0.9914	0.4110	0.4399
APoB/APoA1	0.9469	0.5406	0.4295

*P-value<0.05 is statistically significant*

investigated and assessed in this study. The assessment of these indicators can aid in the prognosis of distant cardiometabolic pathology in this group of women.

From the result obtained in this study, it showed that there was no significant effect of gravidity on the atheriogenic indices of normotensive pregnant women in their second trimester.

Gravidity also showed no significant effect on the atheriogenic indices of hypertensive pregnant women in their second trimester. The findings of this study contradict those of Serrano and Casas [22], who reported that an increase in TG and the ApoB / ApoA1 ratio is linked to an increased risk of pre-eclampsia. In this case there was no significant increase in ApoB/ ApoA1. This disparity could be explained by the fact that this

study looked at pregnant women in their second trimester, whereas several other studies looked at pregnant women in their first and third trimesters. However, a result pattern was observed in this study although the changes were not statistically significant when test. As the number of pregnancies grew, the CRI 1, CRI 2, and AC values decreased, implying that the larger the number of pregnancies, the lower the CRI 1, CRI 2, and AC values for normotensive pregnant women in their second trimester may be.

Similarly, among the gravidity groups, hypertensive pregnant women in their second trimester stage of pregnancy showed a slight and steady drop in their CR-1, CR-2, and AC levels. Although not statistically significant, but owing to similar or repeated arteriogenic pattern among these groups in both normotensive and hypertensive pregnant women in their second trimester of pregnancy, it suggest that increase in number of pregnancy could lead to decrease in arteriogenic indices especially CR-1, CR-2 and AC markers. The loss of significant difference may be due to inequality in the number of subject's distribution among the gravidity groups. A relatively equal number of subject distribution may have provided more logical explanation. This contradicts the findings of Meenakshi et al. [23], who discovered a substantial rise in arteriogenic indices (AIP, CRI, and AC) in the case group compared to the control group ( $p < 0.05$ ) The significance threshold was  $p < 0.0001$ , and assessing arteriogenic indices during pregnancy may help to reduce the risk of cardiovascular disease (CVD). It also does not agree with a study by Aksonova et al. [24], which also demonstrated an increase in AIP, CRI indices in pregnant women with PE in second trimester of pregnancy. There is a paucity of studies on arteriogenic indices in pregnant women in their second trimester [25].

Generally, based on World Health Organization (WHO), [21] reference values for arteriogenic risk classifications, most pregnant women in this study, both normotensive and hypertensive pregnant women among the various groups of gravidity were moderately at risk of arteriosclerosis and cardiovascular disease. Subjects in the primigravida and multigravida groups in both normotensive and hypertensive subjects had high CR-2 level above the WHO cut-off limit ( $>5.0$ ) which made subjects in this group at high risk of arteriosclerosis and CVD [26].

## 5. CONCLUSION

Normotensive and hypertensive women in their second trimester stage of pregnancy may not have expressed significant changes in arteriogenic indices following multiple pregnancies but caution should be emphasized among these women as many arteriogenic indices were at moderate risk level [27].

## ETHICAL CLEARANCE AND CONSENT

The Ethics Committee of the Rivers State Ministry of Health gave their approval. Before being allowed to participate in the study, eligible subjects had to sign a written informed consent form.

## DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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