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Effect of Gravidity on Biochemical Parameters in Normotensives and Hypertensive 2nd Trimester Pregnant Women

Tomaziga Tomiloba Oladapo-Akinfolarin* and Ebirien-Agana Samuel Bartimeus

Department of Clinical Chemistry, Faculty of Medical Laboratory Science, Rivers State University, Port Harcourt, Nigeria

Corresponding author's email address: ola_atomaziga@yahoo.com

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Abstract

The study was aimed at evaluating the effect of gravidity on selected biochemical parameters of cardiovascular disease in normotensive and hypertensive 2nd trimester pregnant women attending antenatal clinics at Rivers State University Teaching Hospital. The 100 consenting subjects who participated in the study were pregnant women in their second trimester. These subjects were randomly selected and divided into two main groups; normotensive pregnant women and hypertensive pregnant women groups. The groups were further divided based on gravidity; primigravida (number of pregnancy=1), multigravida (number of pregnancy>1) and grand multigravida (number of pregnancy≥5). Fasting blood sample was collected using venipuncture method and dispensed into plain bottles for TC, TG, HDL, LDL, ApoA1, ApoB, UA, VLDL and CRP determination. The result represented showed that gravidity had significant impact only on TG, HDL and VLDL among the subgroups, P-value<0.05. While in hypertensive subjects, gravidity had no effect on cardiovascular markers, uric acid level was significant, P-value<0.05. This study has shown that certain lipids are affected due to metabolic changes in 2nd trimester of pregnancy especially in normotensive subjects and these changes increase with increase in gravidity.

Keywords: *Gravidity, pregnancy, cardiovascular marker, hypertensive women, normotensive women*

1.0 Introduction

Gravidity is the number of times a woman has been pregnant [1]. Normal pregnancy is typically divided into three trimesters based on gestational age which is measured in weeks and months. The first trimester is from conception to 12 weeks (2 months and 3 weeks). The second trimester is from 13-27 weeks, (3 months to 6 months and 2 weeks); while the third trimester starts about. 28weeks and lasts until birth (7 months to 9 months) [1].

Pregnancy comes with physiological changes to support foetal growth and development such as lipid metabolic changes [2]. Natural rising of plasma lipids is seen in normal pregnancy, but this event is not Atherogenic and it is believed that, this process is under hormonal control [3], but in complicated pregnancy, there is a possible defect in the mechanism of adjusting physiologic hyperlipidaemia [4]. Lipoproteins are a group of lipids that circulate in plasma in complexes not bound to albumin, low density lipoprotein (LDL), high density lipoprotein (HDL) and very low-density lipoprotein (VLDL) [5]. Plasma lipoproteins are responsible for the transport and delivery of lipids throughout the body [5]. Plasma lipid profiles in the first trimester of pregnancy may predict the incidence and severity of pre-eclampsia [6]. The anabolic phase of early pregnancy encourages lipogenesis and fat storage in preparation for rapid foetal growth in late pregnancy [7]. Lipolysis is increased as a result of insulin resistance, leading to increased flux of fatty acids to the liver promoting the synthesis of very low-density lipoproteins (LDLs) and increased triglyceride (TG) concentrations. Because of a decrease in the activity of lipoprotein lipase, very-LDL remains in the plasma for longer and leads to the accumulation of LDL. An increase in LDL is associated with the development of atherosclerosis [8]. Abnormal lipid metabolism also seems important in the pathogenesis of pregnancy-induced hypertension (PIH). Obviously, the association of serum lipids with gestational proteinuric hypertension is highly suggestive of a role for lipid profile analysis as a diagnostic tool [9].

During the course of normal pregnancy, plasma triglyceride and cholesterol concentrations rise and as pregnancy progresses both become normal [2].
Another hypothesis is that hypertriglyceridemia is probably a consequence of competition between chylomicrons and very LDL cholesterol for the lipoprotein lipase. The conclusion of another study also indicated that there exists a consistent positive association between elevated maternal TG and the risk of pre-eclampsia. [10].

Hypertension in pregnancy induces long term metabolic and vascular abnormalities that might increase the overall risk of cardiovascular, cerebrovascular and kidney diseases as well as diabetic mellitus later in life [11]. It is therefore imperative to investigate the effect of gravidity on most of the biochemical parameters in normotensive and hypertensive 2nd trimester pregnant women.

2.0 Materials and Methods

2.1 Study Design

The cross-sectional study conducted at Rivers State University Teaching Hospital, Port Harcourt was designed with the participation of 100 pregnant women in their second trimester of pregnancy. These 100 subjects were divided into two main groups; normotensive (n=50) and hypertensive (n=50) based on their clinical folder report. Each of the main groups were further divided into three subgroups; primigravida (number of pregnancy=1), multigravida (number of pregnancy>1) and grand multigravida (number of pregnancy≥5). Normotensive subgroups had the following subject participation; primigravida (n=15), multigravida (n=27) and grand multigravida (n=8) while hypertensive subgroups had the following; primigravida (n=21), multigravida (n=21) and grand

multigravida (n=4). The data generated were compared among the subgroups for each group.

2.2 Ethical consideration and consent

The Ethics Committee of Rivers State Ministry of Health provided the ethical approval for the study while the subjects provided written consent to participate in the study.

2.3 Study Eligibility

All subjects registered in the facility (Rivers State University Teaching Hospital) for antenatal purpose were included in the study having provided written consent to participate in the study but subjects assessing other form of healthcare service other than antenatal care were not included. Also, subjects with unconfirmed pregnancy such as fibroid growth perceived to be pregnancy were excluded.

2.4 Sampling Method

Simple sampling technique that employed the use of selection of numbers between "0" and "1" was adopted, such that subjects who picked '0" were not selected while subjects who picked "1" were selected [12,13].

2.5 Sample collection method

Sample for analysis collected was blood. The sample was collected in fasting condition via venipuncture technique. The collected sample was dispensed in plain bottle, allowed to clot, spun to separate the serum and store in refrigerator at $4^{o}C$ until the time for analysis [14,15].

2.6 Laboratory Methods

Determination of Total Cholesterol in Serum
Total cholesterol was measured quantitatively by enzymatic method [16].

Determination of High-Density Lipoprotein (HDL) Cholesterol in Serum
HDL-C was measured quantitatively by enzymatic method ([17].

Determination of Triglycerides in Serum
Triglycerides are determined quantitatively by enzymatic method [18].

Determination of Low-Density Cholesterol (LDL-C)

LDL cholesterol was calculated from the Friedewald's equation [19].

LDL – Cholesterol = Total Cholesterol – (TG/2.2) – HDL

Determination of Apo Lipoprotein A1 in Human Serum
Apolipoprotein A1 was measured quantitatively by turbidimetric method [20] as described by Fortress Diagnostics Limited (United Kingdom).

Determination of Apolipoprotein B in Human Serum

Apolipoprotein B was measured quantitatively by turbidimetric method [20] as described by Fortress Diagnostics Limited (United Kingdom).

Determination of Uric Acid in Serum

Uric acid was determined quantitatively by enzymatic method [21] as described by Randox Laboratories Limited (United Kingdom).

Determination of High Sensitive C-reactive Protein Concentration in Human Serum.

C-reactive protein was measured quantitatively by turbidimetric method [20] as described by Fortress Diagnostics Limited (United Kingdom).

2.6 Statistical Analysis

The data gathered in this study was statistically analyzed for descriptive statistics for mean±SD and inferential statistics (ANOVA) using SPSS version 23.0. Level of significance was set at $P<0.05$.

3.0 Results

Table 1.0 (a) shows the effect of gravidity on biochemical parameters among normotensive pregnant women in their 2^{nd} trimester. The result show that there was a significant difference in TG

among the gravidity groups (primigravida, multigravida and grand multigravida), P-value <0.05. Also there was a significant difference in HDL and VLDL among the gravidity groups, P-value <0.05. Other parameters studied had no significant difference, P-value >0.05.

Table 1.0(a): Effect of Gravidity on Biochemical Parameters in Normotensives 2nd Trimester

Parameters	Normotensive women			P-value	F-value
	Primigravida (1) N=15	Multigravida (>1) N=27	Grand Multigravida (≥5) N=8		
TC(mmol/l)	4.31 ± 0.33	4.37 ± 0.50	4.46 ± 0.59	0.7706	0.2617
TG (mmol/l)	1.15 ± 0.18	1.32 ± 0.22	1.50 ± 0.28	**0.0023**	0.9320
HDL(mmol/l)	0.76 ± 0.15	0.89 ± 0.20	0.96 ± 0.23	**0.0441**	0.9320
LDL (mmol/l)	3.05 ± 0.22	2.92 ± 0.47	2.84 ± 0.37	0.3990	0.9369
APoA1 (mg/dl)	340.90 ± 20.71	341.50 ± 40.90	348.50 ± 40.92	0.8737	0.1354
APoB (mg/dl)	131.40 ± 15.43	130.40 ± 26.83	136.30 ± 21.13	0.8803	0.1278
CRP(mg/L)	3.85 ± 1.17	4.63 ± 1.76	4.05 ± 0.82	0.2155	1.5860
VLDL (mmol/l)	0.52 ± 0.08	0.60 ± 0.10	0.68 ± 0.13	**0.0023**	6.9310
UA (mg/dl)	5.03 ± 0.40	5.13 ± 0.42	4.99 ± 0.49	0.6183	0.4857

Table 1.0(b) shows the comparison of gravidity between groups. The comparison shows that comparison between primigravida and grand multigravida was statistically significant in TG values between both groups, P-value<0.05. Similarly, the comparison between primigravida and grand multigravida was statistically significant in VLDL values between both groups, P-value<0.05. Other comparisons were not statistically significant, P>0.05.

Table 1.0(b): The ANOVA Post – Hoc Findings Using Turkey Multiple Comparison Test for Effect of Gravidity on Biochemical parameters (Normotensive 2nd Trimester)

Parameters	Primagravida vs. Multigravida	Primagravida vs Grand multigravida	Multigravida vs Grand Multigravida
TC(mmol/l)	0.9253	0.7515	0.8786
TG (mmol/l)	0.0511	**0.0019**	0.1160
HDL(mmol/l)	0.1224	0.0543	0.5867
LDL (mmol/l)	0.5263	0.4322	0.8784
APoA1 (mg/dl)	0.9988	0.8816	0.8796
APoB (mg/dl)	0.9952	0.8801	0.8948
CRP(mg/L)	0.2173	0.9432	0.5776
VLDL (mmol/l)	0.0511	**0.0019**	0.1161
UA (mg/dl)	0.7355	0.9761	0.6879

Table 2.0 (a) shows the effect of gravidity on biochemical parameters among hypertensive pregnant women in their 2nd trimester. The result show that there was no significant difference in the studied parameters among the gravidity groups (primigravida, multigravida and grand multigravida), P-value >0.05. However, there was a significant difference in UA among the gravidity groups, P-value <0.05.

Table 2.0 (a): Effect of Gravidity on Biochemical Parameters in Hypertensive 2nd Trimester

Parameters		Hypertensive Women		P-value	F-value
	Primigravida (1) n = 21	Multigravida(>1) n = 25	Grand Multigravida (≥ 5) n = 4		
TC(mmol/l)	4.86 ± 0.37	4.96 ± 0.32	4.80 ± 0.23	0.5109	0.6812
TG (mmol/l)	1.53 ± 0.33	1.57 ± 0.28	1.70 ± 0.35	0.6074	0.5039
HDL(mmol/l)	0.93 ± 0.20	0.99 ± 0.22	1.10 ± 0.12	0.2919	1.6240
LDL (mmol/l)	3.23 ± 0.29	3.24 ± 0.24	2.95 ± 0.06	0.1148	2.2670
APoA1 (mg/dl)	361.60 ± 26.96	361.40 ±29.82	358.50 ±15.59	0.9789	0.0214
APoB (mg/dl)	122.30 ± 14.41	121.00 ± 12.24	127.00 ± 5.77	0.6904	0.3735
CRP(mg/L)	7.61 ± 2.04	7.28 ± 1.75	7.50 ± 1.27	0.8293	0.1879
VLDL (mmol/l)	0.70 ± 0.15	0.71 ± 0.13	0.77 ± 0.16	0.6074	0.5039
UA (mg/dl)	4.81 ± 0.30	4.67 ± 0.40	4.25 ± 0.29	**0.0200**	4.254

Table 2.0(b) shows the comparison of gravidity between groups. The comparison shows that comparison between primigravida and grand multigravida was statistically significant in UA values between both groups, P-value<0.05. Other comparisons were not statistically significant, P>0.05.

Table 2.0(b): The ANOVA Post – Hoc Findings Using Turkey Multiple Comparison Test for Effect of Gravidity on Biochemical parameters (Hypertensive 2nd Trimester)

Parameters	Primagravida vs. Multigravida	Primagravida vs Grand multigravida	Multigravida vs Grand Multigravida
TC(mmol/l)	0.5938	0.9454	0.6671
TG (mmol/l)	0.9054	0.5841	0.7209
HDL(mmol/l)	0.5699	0.3155	0.6250
LDL (mmol/l)	0.9993	0.1176	0.1072
APoA1 (mg/dl)	0.9999	0.9778	0.9791
APoB (mg/dl)	0.9433	0.7826	0.6700
CRP(mg/L)	0.8159	0.9930	0.9736
VLDL (mmol/l)	0.9054	0.5841	0.7209
UA (mg/dl)	0.5030	**0.0152**	0.0625

4.0 Discussion

From the result gotten, triglyceride (TG) was significantly higher in grand multigravida compared with primigravida and multigravida (p=0.0023) of normotensive pregnant women at 2nd trimester. High Density Lipoprotein (HDL) was also significantly higher in grand multigravida compared with primigravida and multigravida (p=0.0441) of the normotensive pregnant women at 2nd trimester. Very Low Density Lipoprotein (VLDL) was significantly higher in grand multigravida compared with primigravida and mutigravida (p=0.0023). This indicates that the higher the number of pregnancy, the higher the TG, HDL and VLDL concentrations in normotensive pregnant women at 2nd trimester. Using Turkey multiple comparison, it showed that TG was significantly higher when grand multigravida was compared with primigravida of Normotensive pregnant women at 2nd trimester (p=0.0019). VLDL was also significantly higher in grand multigravida of Normotensive pregnant women at 2nd trimester compared with primigravida of Normotensive pregnant women at 2nd trimester (p=0.0019) indicating that the higher the number of pregnancy, the higher the concentration of TG and VLDL. The result also showed that gravidity had no effect on other biochemical parameters such as Total Cholesterol (TC), Low density Lipoprotein (LDL), ApoA1, ApoB, C-reactive protein (CRP) and Uric Acid (UA). Gravidity were found to be positively associated with prevalence of metabolic syndrome and multiparus women have increased risk of developing metabolic syndrome according to Dabou et al. [22].

The results from this work agrees with Siddiqui, [23] that there are no statistical differences in TC, and LDL in Normotensive women and therefore not related with the disease, and that TG increased statistically in normotensives and that the increase is involved in endothelial damage leading to preeclampsia.

In this study, TG, HDL and VLDL were statistically increased in Normotensive at $p < 0.05$. It also disagrees with Bayhan *et al*. [24] who assessed 25 pregnant women that developed mild preeclampsia, 28 pregnant women that developed severe preeclampsia and 25 pregnant women in a control group, during the third trimester and found a significant decrease in HDL levels in patients that developed preeclampsia.

The result further showed that gravidity brought about a significant reduction in UA concentration in multigravida and grand multigravida of pregnant women at 2nd trimester compared with primigravida of pregnant women at 2nd trimester (p=0.0200). This suggests that the higher the number of pregnancy, the lower the Uric acid Concentration. Using Tukey multiple comparison, UA was significantly lower in grand multigravida of hypertensive pregnant women at 2nd trimester compared with primigravida of hypertensive pregnant women at 2nd trimester (p=0.0152) at $p<0.05$ while gravidity had no effect on other biochemical parameters.

This work disagrees with Enquobahrie *et al*. [25] that there was a significant rise in LDL concentration in the preeclamptic women than in normal pregnant women. However, this work agrees with Enquobahrie [26] and Clausen [27] that there was no significant difference in mean total cholesterol concentration in the preeclamptic group when compared with that in normal pregnant group. The finding in this work agrees with Tam *et al*. [28] that maternal serum uric acid concentration was a good prognostic factor for monitoring, and prognosis of fetal/neonatal outcomes in women with preeclampsia/eclampsia. There was a relationship between high uric acid level and the risk of preterm birth, low Apgar index, and neonatal death, but not fetal death. Contrarily, the level of significance in this work was a decreased value of uric acid in hypertensive pregnant women.

Preeclampsia is characterized by inflammation, although the onset is placental origin, a network of unfavourable responses is released, this inflammatory responses is

complex involving multiple cytokines such as interleukin 6 and tumor necrosis factor– α which are elevated in preeclampsia. These cytokines support the expression of the acute – phase protein C-reactive protein. According to Mohaupt [29], an increase in CRP is associated with preeclampsia. The author demonstrated the placenta as the production site for CRP in addition to the liver in non-pregnant conditions but infused CRP at a concentration comparable to those found in the circulation of preeclamptic women into mice, which led to hypertension, glomerular damage and associated proteinuria as well as to features of premature atherosclerosis within the placenta. This disagrees with the result of this research that the CRP values increases, but there was no significant effect in the CRP concentration. Rebelo *et al*. [30] also showed a positive association between CRP levels and development of preeclampsia, though admonished that other factors should be considered.

The parameters Apo A1, Apo B and Apo B / ApoA1 were not significant at $p < 0.05$. These values disagree in part with Timur *et al.* [31]. In their work on the Apolipoprotein levels in women with preeclampsia, they found out that Apo B and Apo B / Apo A1 were significantly increased, but Apo A1 was significantly decreased and advocated that Apo A1 and Apo B/Apo A1 ratio be useful markers in patients with preeclampsia.

Conclusion

Changes in lipid profile in pregnancy is a long existing fact, however, this study has not only pointed to the fact that these lipid cardiovascular markers change in pregnancy but some of these markers increase with increasing gravidity, therefore, it is important that cardiovascular risk assessment be included in antenatal clinics.

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