ORIGINAL ARTICLE

Plasma Lipids During Pregnancy In Women In Port Harcourt, Nigeria

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ABSTRACT

Background: *Pregnancy in Caucasian women is known to be associated with hyperlipidaemia. In a background of poor socio-economic conditions, early marriage, poor acceptance of contraceptives, poor spacing of pregnancies, high fertility rate and poor maternal and child health indices, this study was designed to investigate the pattern and degree of serum lipid changes during pregnancy in black African women in Port Harcourt, Nigeria.*

Methods: *Two hundred and thirty apparently healthy pregnant women at different stages of pregnancy and 51 non-pregnant control subjects of comparable age, height, and parity were serially recruited into the study. Plasma total cholesterol (TCHOL), LDL-Cholesterol (LDL-CHOL), HDL-Cholesterol (HDL-CHOL) and triglycerides (TG) were estimated for all study subjects and mean plasma lipid levels calculated for first, second and third trimesters of pregnancy.*

Results: *There was an increase in the mean concentration of plasma TCHOL, HDL-CHOL, and TG and a decrease in LDL-CHOL in the pregnant subjects as compared to the non-pregnant control subjects. Mean TCHOL, HDL-CHOL, LDL-CHOL and Triglycerides tended to increase with increasing gestational age.*

Conclusion*: The results show that pregnancy in black Nigerian women is associated with hyperlipidaemia. The implications of this finding are discussed.*

KEY WORDS: *Plasma lipids; Pregnancy; Port Harcourt.*

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INTRODUCTION

Current interest in plasma lipids stems from the association between high blood lipid concentrations and the risk of cardiovascular disease in several large population studies[1]. Pregnancy is a physiological state that is recognized to be consistently associated with hyperlipidaemia [2-4]. These alterations in lipid metabolism may be due to many factors associated with pregnancy. However, sex steroids (oestrogens, progestogens and androgens) are thought to play a major role [1,5-7]. These sex steroids are known to affect the activities of hepatic and extra hepatic lipoprotein lipases, which control the access of various lipoproteins into the blood circulation, hence altering their plasma concentrations[6,7]. It is well established that pregnancy is characterized by five to ten fold rises in the circulating levels of oestrogens, progestogens and androgens [8,9]. These effects may be contributory to the changes in lipid metabolism seen during pregnancy.

Most of the studies relating to changes in lipid metabolism during pregnancy have been done in Caucasians and other non-Negro populations [1-9]. Plasma lipid levels are known to be influenced by several factors, apart from pregnancy [1]. These include age, sex, diet, obesity, exercise, alcohol, smoking, drug therapy, race, genetic, environmental and socio-economic factors and certain disease states[10].

African women start childbearing at an earlier age and they have demonstrated a higher fertility rate and higher number of pregnancies before menopause than Caucasians. Moreover, the socio-economic and socio-cultural factors are different for African compared with Caucasian women. Thus results of observations on lipid metabolism done on pregnant Caucasian women may, therefore, not be directly extrapolated to pregnant African women. There is a paucity of information on lipid changes during pregnancy in black female Africans. The few studies available give conflicting information, with some reporting an increase [10,11] or a decrease [11,12] in plasma lipids or their fractions during pregnancy.

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We therefore undertook this study to investigate the pattern of plasma lipid changes during pregnancy in a purely African Negro population in Nigeria, with a view to contributing more information in this area of research.

PATIENTS AND METHODS

Two hundred and thirty apparently healthy patients (mean age = 28.2 ± 4.8 years) at different stages of pregnancy were recruited into the study from the antenatal clinic of the University of Port Harcourt Teaching Hospital, Port Harcourt. They consisted of 35 patients in the first trimester, (89) patients in the second trimester and 106 patients in the third trimester of pregnancy. Similarly, 51 age-matched (mean= 26.8 ± 3.4 years), apparently healthy non-pregnant subjects consisting of Hospital staff and students were recruited into the study as control subjects.

All subjects with history of endocrine disease, liver disease, chronic illness or other diseases likely to cause alterations in plasma lipid concentrations were excluded from the study. Informed consent was obtained from all subjects before recruitment.

During the course of clinic attendance, all relevant data including age, parity, gestational age, height and weight were extracted from the patients' case notes. Then 5millilitres of blood was obtained from each patient by venepuncture of the ante-cubital veins and transferred into plain specimen bottles (without anticoagulant). At the end of each clinic session (9.00 am - 12.00 noon) all blood samples were taken to the Chemical Pathology laboratory. The specimens were then centrifuged for 10 minutes at 3000 rpm. Serum was transferred into plain storage tubes and sample was stored at 20°C in a deep freezer until analyzed. During the course of the study, samples were similarly obtained and processed from the non-pregnant control subjects following personal contact and informed consent.

All samples were batch-analyzed within 3 weeks of collection. Routine accuracy and precision quality control samples were included in each batch of the analyses. All analyses were done using kits manufactured by SEAC (via di prato, 74 0-50041, Calenzano, firenze, Italy). Triglycerides (TG) were estimated by the colorimetric Glycerol phosphate oxidase method [13,14]. Total cholesterol (TCHOL) was estimated by the enzymatic cholesterol esterase/cholesterol oxidase method [14,16]. HDL Cholesterol (HDL-CHOL) was estimated by the enzymatic cholesterol esterase/cholesterol oxidase method (above) after selective precipitation of the serum lipid fractions (LDL, VLDL and chylomicron) using a solution of phospotungstic acid and magnesium chloride as precipitating reagent [17,18]. LDL-Cholesterol was calculated by the Friedwald formula [19].

LDL- CHOL = TCHOL(TG/2.2) - HDL-CHOL (mmol/L).

The data was analyzed with an SPSS statistical package in a personal computer. Group means were compared by the unpaired Student's 't' test. $P < 0.05$ was regarded as statistically significant.

RESULTS

The characteristics and serum lipid concentrations of the study subjects are as shown in Table I. and illustrated in Figure 1. Table I. shows that both the pregnant and non-pregnant control subjects are comparable in terms of age, height, weight and body mass index (B.M.I), taking into consideration the effect of pregnancy on body weight and BMI.

Inspection of Table I shows that out of the 230 pregnant study subjects, only 35 were in their first trimester. This clearly demonstrates the fact that in Africa, pregnant women do not book early for antenatal care. The situation is even worse in the rural areas where pregnant women only go to ' register' in health centres late in their third trimester in anticipation of imminent delivery. This results largely from ignorance about the benefits of early booking and antenatal care.

Total Cholesterol (TCHOL)

Mean serum TCHOL was significantly higher in pregnant subjects (as a group) as compared to non-pregnant control subjects (5.4 ± 1.3 vs. 5.1±1.0 mmol/L, $P<0.05$). However, the mean TCHOL of first trimester subjects was

significantly lower than that of the non-pregnant subjects (4.3 ±1.2 vs 5.1± 1.0 mmol/L, P<0.05). Thereafter, there was a gradual rise in mean serum TCHOL from first trimester (4.3 ±1.2 mmol/L) to 2nd trimester (5.3 ± 1.2 mmol/L) and to 3rd trimester (5.8 ± 1.3 mmol/L). The difference between the mean value of first and second trimester subjects was statistically significant (4.3 ±1.2 vs 5.3 ± 1.2 mmol/L, P<0.05) while the difference between second and third trimester subjects was also statistically significant (5.3 ± 1.2 vs 5.8 ±1.3 mmol/L, P<0.05)

HDL-Cholesterol (HDL-CHOL)

The mean serum HDL-CHOL was significantly higher in pregnant subjects as compared to the non-pregnant control subjects (1.8 ± 0.7 vs 1.6 ± 0.6 mmol/L, P<0.05). However, the mean serum HDL-CHOL for first trimester subjects was significantly lower than that of the non-pregnant control subjects (1.0 ± 0.5 vs 1.6 ± 0.6 mmol/L, P<0.05), indicating a lowering of HDL-CHOL with the onset of pregnancy. There was a significant increase from the first to the second trimester, with the second trimester mean HDL-CHOL being significantly higher than that of the first trimester (2.0 ± 0.7 VS 1.0 ± 0.5 mmol/L, P<0.05). The mean serum HDL-CHOL thereafter seemed to remain almost constant during the second and third trimesters, with a tendency to a slight fall during the third trimester (2.0 ± 0.7 and 1.9±0.06 mmol/L, respectively, P> 0.05).

These results suggest an initial lowering of serum HDL-CHOL with the onset of pregnancy, followed by a sustained rise during the second and third trimesters.

LDL-Cholesterol (LDL-CHOL)

Mean serum LDL-CHOL was significantly lower in pregnant subjects as compared to the non-pregnant control subject (2.8 ± 1.0 vs 3.7 ± 0.9 mmol/L, P<0.05). The mean LDL-CHOL was significantly lower in first trimester subjects as compared to the non-pregnant control subjects (2.9 ± 1.2 vs 3.7± 0.9 mmol/L, P< 0.05), indicating a significant decrease in plasma LDL-CHOL with the onset of pregnancy. Thereafter, the plasma LDL-CHOL dropped further to a mean of 2.5 ± 1.0 mmol/L during the second trimester. The difference between the first and second trimester levels was statistically significant (P<0.05). By the third trimester a statistically significant rise had occurred, from the second trimester mean of 2.5 ± 1.0 mmol/L to a third trimester mean of 3.0 ± 1.0 mmol/L (P<0.05). These results suggest an initial drop in plasma LDL levels with the onset of pregnancy, followed by a gradual return to pre-pregnancy levels towards the end of pregnancy.

Triglycerides (TG)

The mean plasma TG was significantly higher in pregnant subjects as compared to the non-pregnant control subjects (1.8 ± 0.7 vs. 0.7 ± 0.2 mmol/L, P<0.05). The results show a gradual increase in mean plasma TG from the first trimester (0.9 ± 0.3 mmol/L) through the second trimester (1.7 ± 0.6 mmol/L) to the third trimester(2.1±0.7 mmol/L). The increases between the trimesters were all statistically significant (P<0.05).

These results suggest a significant progressive increase in mean plasma triglyceride with increasing gestational age.

Correlation Studies

In further analyzing the results of this study, correlation studies were done between the various anthropometric and lipid parameters, as follows:

Parity: There was weak correlation (r<0.2) between parity and BMI, HDL-CHOL, LDL-CHOL and TG for both the pregnant and non-pregnant control subjects. However, there was no correlation between parity and TCHOL (r=0.08), suggesting that the parity of a woman may influence some of her plasma lipid parameters (HDL-CHOL, LDL-CHOL and TG) but not TCHOL.

Age: For the pregnant subjects there was weak correlation between Age/TCHOL (r= 0.1), Age/LDL-CHOL (r = 0.2), Age/TG(r = 0.2), and Age/BMI (r = 0.2). For these pregnant subjects, there was no correlation between Age/HDL-CHOL.

In the non-pregnant control subjects, there

was significant correlation between Age/BMI (r= 0.7). For these non-pregnant control subjects, there was no significant correlation between age and all the lipid parameter (TCHOL, HDL-CHOL, LDL-CHOL, and TG).

These results suggest that in non-pregnant Nigerian females, BMI increases with age, but the age of an individual may not influence absolute plasma lipid levels. However, during pregnancy, increased maternal age may be associated with increase in absolute plasma levels of maternal TCHOL, LDL-CHOL, and TG. That this finding may be contributing to the poorer obstetric outcomes observed in elderly pregnant females remains largely speculative.

Gestational Age (GA): There was strong positive correlation between GA/TG(r=0.5) GA/TCHOL (r=0.4) and GA/HDL-CHOL (r=0.4) in the pregnant subjects. However, there was no correlation between GA/LDL-CHOL. This result further suggests a progressive rise in TG, TCHOL and HDL-CHOL with advancing gestational age.

BMI: For the pregnant and non-pregnant control subjects, there was significant correlation between BMI/TCHOL ($r \geq 0.3$), BMI/LDL-CHOL ($r \geq 0.3$) and BMI/TG($r \geq 0.4$), but no correlation between BMI/HDL-CHOL. These results suggest increased plasma lipid fractions with increasing BMI in pregnant and non-pregnant subjects.

Table I. Characteristics And Serum Lipid Concentrations Of Study Subjects

Mean (SD)

	1st Trimester	2nd Trimester	3rd Trimester	Pregnant Subjects	Control
Number	35	89	106	230	51
Age (yrs)	30.66(3.77)	27.55(4.08)	27.91(5.36)	28.19(4.78)	24.80(3.29)
Parity	1.06(1.07)	1.26(1.59)	1.40(1.84)	1.29(1.65)	0.20(0.72)
Weight (kg)	69.73(11.53)	72.57(9.88)	76.55(11.24)	73.97(11.04)	63.52(9.48)
Height (m)	1.65(0.08)	1.62(0.07)	1.62(0.06)	1.62(0.07)	1.65(0.06)
BMI (Kg/m^2)	26.18(4.03)	27.69(2.87)	29.25(4.15)	28.18(3.82)	23.37(3.68)
TCHOL (mmol/L)	4.27(1.18)	5.32(1.22)	5.84(1.25)	5.43(1.33)	5.10(1.01)
HDL-CHOL (mmol/L)	1.01(0.53)	2.00(0.67)	1.94(0.61)	1.84(0.70)	1.59(0.55)
LDL-CHOL (mmol/L)	2.85(1.15)	2.52(1.00)	2.97(0.99)	2.77(1.03)	3.67(0.89)
Triglycerides (mmol/L)	0.91(0.29)	1.71(0.61)	2.09(0.68)	1.78(0.72)	0.68(0.23)

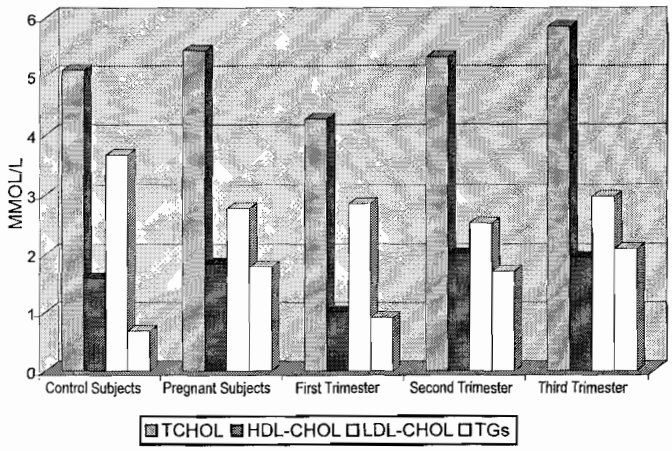

Fig. 1. Variations Of Plasma Lipid Levels With Gestational Age

DISCUSSION

The results of this study demonstrate that pregnancy in Nigerian Negro women is also associated with hyperlipidaemia, as seen in Caucasians[2-4]. This is demonstrated by a consistent statistically significant increase in all lipid fractions assayed (except LDL-CHOL) in the pregnant subjects as compared to the non-pregnant control subjects.

This finding is in general agreement with previous reports in pregnant Nigerian Negro women [10-12], although with important differences in the pattern of variation in some plasma lipid fractions.

While this study demonstrated a mild reduction in LDL-CHOL with an increase in HDL-CHOL, a recent study by Jarikre and Ola[11] in Lagos reported an increase in LDL-CHOL with a reduction in HDL-CHOL during pregnancy. This may not be entirely surprising as such differences in the variation of plasma lipid fractions have also been noted in Caucasian populations. For example, Sitadevi *et al* reported an increase in TCHOL [20], while de Alvarez *et al.* [21], reported a decrease in TCHOL during the first trimester of pregnancy. In Nigerian women, Ola and Adedeji [12] had reported normal TCHOL in the first trimester of pregnancy, as compared to non-pregnant control subjects. As already noted by Jarikre and Ola[11], these conflicting results seem to suggest that the exact pattern of variation of plasma lipid fractions during normal pregnancy

in both Negroes and Caucasians may be variable. However, all previous studies, including the present study, demonstrate unequivocally that pregnancy is associated with hyperlipidaemia.

Hyperlipidaemia is established as a risk factor for cardiovascular disease [22]. The results of this study demonstrate that pregnancy in black Nigeria women is associated with hyperlipidaemia. African women are known to have a high fertility rate in a socio-economic environment that is characterized by a high degree of illiteracy, ignorance, poverty and disease. Early sexual activity [23], early marriage and commencement of child bearing at early tender ages are prominent features of women's health in Africa.

Contraception is a relatively recent phenomenon in Africa and is not yet as widely accepted as in developed western countries [24, 25]. Moreover, contraception may not be culturally acceptable to most indigenous black African women, especially the greater majority in the rural area [26]. Hence, many start child bearing from menarche until menopause, with little or no spacing between pregnancies, some having as many as 12 to 15 pregnancies during the reproductive period of their lifetime.

The deleterious effects of hyperlipidaemia are associated with persistent, rather than transient high plasma lipid levels [22]. This translates to high cumulative mean plasma lipid levels over time. The higher the mean plasma lipid levels, the higher the risk of cardiovascular and other lipid-related diseases [22]. The African society is associated with a high fertility rate and high parity, with little or no spacing between pregnancies. The results of this study clearly demonstrate that these pregnancies lead to states of relative hyperlipidaemia.

It is therefore reasonable to speculate that fertile African women are exposed to higher than normal mean plasma lipid levels over time as a result of frequent pregnancies.

In Africa, maternal mortality rate has remained high. The lifetime risk of dying from pregnancy or childbirth-related causes can be as high as 1 in 20 in developing countries of Africa compared to 1 in 10,000 in some developed countries in Europe and North America [27]. This high maternal mortality rate has been traditionally attributed to several socio-economic and socio-cultural factors [27]. In the light of the results of this study, it may be worthwhile to ask if the hyperlipidaemia of frequent pregnancies may be adversely affecting the health of African women and contributing to high maternal mortality rate in Africa.

The pattern of hyperlipidaemia seen in this study is interesting with respect to the epidemiological evidence linking the various lipid fractions to adverse health outcomes. Epidemiologically, high plasma levels of TCHOL, LDL-CHOL, and TGs have been linked to greater risk of cardiovascular disease, while high HDL-CHOL levels are associated with a lowered risk [22].

This study has demonstrated that pregnancy in African women may be associated with increased plasma levels of TCHOL and TGs, which confer an adverse risk profile, while at the same time, these pregnancies are also associated with reduced plasma LDL-CHOL and increased plasma HDL-CHOL levels, which are associated with a reduced cardiovascular risk profile.

Where does the balance lie? Does the hyperlipidaemia of frequent pregnancies impose an extra risk of cardiovascular or other lipid-related diseases in African women? Is pregnancy in African women associated with an increased risk or a decreased risk of cardiovascular disease due to these changes in the plasma lipid fractions? Or do these opposing effects cancel out, with the hyperlipidaemia of pregnancy not significantly affecting the risk for cardiovascular or other lipid-related disease in African women?

These questions clearly indicate the need for more focused research on plasma lipid changes and their health effects during pregnancy in African women, as part of the on-going effort towards improved reproductive health care delivery in sub-Saharan Africa.

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