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TERTIARY HEALTH INSTITUTION, SOUTHWEST NIGERIA**

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ABSTRACT

Introduction: Plasma lipid concentrations increase markedly during pregnancy due to estrogen stimulation and insulin resistance. This study aimed to assess the lipid profile parameters in apparently normal pregnant women.

Methods: The study was a comparative cross sectional study carried out among ninety-six consecutive pregnant women in all trimesters of pregnancy. Participants were selected by simple random technique during the antenatal clinic days with informed consent. Clinical assessments including weight, height and body mass index (BMI) were determined. 5mls blood specimens was collected for the fasting lipid profile into lithium heparin sample bottles and plasma was separated into a plain bottle and frozen at -20°C until assay time. Data were analyzed using SPSS version 20.

Results: The mean total cholesterol (6.26 ± 1.44 vs. 4.44 ± 1.01 mmol/L, $P=0.001$), LDL-c (4.54 ± 1.40 vs. 3.21 ± 0.87 mmol/L, $p=0.010$) and Triglycerides (1.26 ± 0.47 vs. 0.52 ± 0.27 mmol/L, $p<0.001$) were significantly higher during pregnancy. The total cholesterol and LDL-c were highest in the third trimester while the increase in triglycerides was more in the first trimester with only a modest increase in the second and third trimesters.

Conclusion: All the lipid profile parameters were higher in pregnant women but with different patterns. The total cholesterol (T.chol), low-density lipoprotein cholesterol (LDL-c) and triglyceride increase progressively from the first to the third trimester while the high-density lipoprotein cholesterol (HDL-c) demonstrated an initial increase in the first trimester with a fall in the second trimester before a final rise in the third trimester.

Keywords: lipid profile, dyslipidemias, pregnancy, atherosclerosis, cardiovascular disease

INTRODUCTION

Pregnancy is a physiological process associated with changes including cellular and tissue adaptations to cope with the increased metabolic demand by both the mother and the growing fetus. Advancement of pregnancy is accompanied by the extra demand for energy. As pregnancy progresses, a well-integrated metabolic shift occurs to ensure a sufficient supply of nutrients to a constantly feeding fetus from an intermittently fasting and feeding mother.¹

Early in pregnancy, various hormonal changes occur including a rise in serum levels of estrogen and progesterone, as well as pancreatic beta-cell hyperplasia which leads to an increase in the secretion of

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insulin.² Hyperinsulinemia usually brings about an increase in peripheral glucose utilization, a decline in fasting plasma glucose levels, increased tissue storage of glycogen, increased storage of fats and decreased lipolysis. Maternal metabolic changes in pregnancy have been described as “accelerated starvation” when food is unavailable and “facilitated anabolism” when food is ingested.³

Later in pregnancy, metabolic adaptations spare glucose for the fetus and cause a switch from carbohydrate to fat metabolism as an alternative source of energy for the mother leading to an increased concentration of plasma lipids. This increase has been attributed to a decrease in maternal glucose insulin sensitivity.⁴ Also, it is known that high concentrations of steroids occur as normal pregnancy advances. Since cholesterol is the source of most of the steroids found in increased amounts in the circulation of normal pregnant patients, the part played by lipid metabolism in pregnancy, becomes all the more intriguing – as cholesterol is a major factor in the development of atherosclerosis.⁵

One of the earliest reports of changes in lipid profile in pregnancy was done by Chauffard in 1911 when he suggested an increase in cholesterol level.⁶ With the development of more modern techniques, various studies observed an increase in various lipid fractions, though the increase was neither consistent in terms of appearance nor proportion of changes in various fractions. Most authors believe that the increase in blood lipids is related to the requirements of the fetus and to the development of the mammary apparatus.⁶

A study by Idonije *et al* observed that the concentration of serum total cholesterol, serum triglyceride, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol in normal pregnant women increased with increasing gestational age although high-density lipoprotein dropped a little in the 2nd trimester with the serum triglyceride concentration showing a very

significant increase in the third trimester of normal pregnancy than in the nonpregnant women, the mean value being raised almost two folds.⁷

Therefore, dyslipidemia appears to be a common prenatal finding but not quite much has been reported in this study area. Thus, in the present study, an attempt was made to define more precisely the changes in lipid fractions during different periods of gestation.

METHOS

Study design and area

The study was a comparative cross-sectional design carried out at the Ladoke Akintola University of Technology Teaching Hospital (LTH) Ogbomoso, Oyo State, Nigeria. Ogbomoso is estimated to have a population of about a 1.2million people majority of whom are of the Yoruba ethnic group. Ogbomoso is the second largest city in Oyo state after the capital city of Ibadan.⁸

Study population and size

Ninety-six consecutive pregnant women in all trimesters of pregnancy, all recruited during ante-natal clinics were stratified as follows: 24 pregnant women in the first trimester, 39 in second trimester and 33 in the third trimester. The controls were one hundred nonpregnant women between the ages 18 and 45 years. The total sample size studied was one hundred and ninety-six.

Sampling

Participants were selected by simple random technique during the antenatal clinic days. The control participants were recruited from the staff of the hospital, patients’ relatives and willing community residents. Verbal and written informed consents were obtained after a careful explanation of the study to them and the study questionnaire was administered to each participant to obtain biodata and other relevant information. Selection and recruitment for the study continued until the desired sample size was met. The controls were age-matched apparently well non-pregnant women.

Procedure

Clinical assessment was performed on all subjects; weight, height and body mass index (BMI) were determined for each subject. The body surface area was also calculated using the formula:

$$BSA = 1/6(\text{Weight} \times \text{Height})^{0.5}$$

5mls of peripheral venous blood of both groups, pregnant women and non-pregnant controls, was collected for fasting lipid profile into sample bottles containing lithium heparin anti-coagulant. Each sample was centrifuged at 3,000 rpm x g for 10 – 15 minutes using Everich centrifuge model 80-2; the centrifuge speed was routinely checked with a strobe tachometer as well as the timer according to the College of American Pathologists (CAP) guidelines. The plasma and serum obtained were aliquoted into screw cap plane bottle and stored frozen at -20°C. The temperature of the freezer was monitored with daily check and recording of National Institute of Standards and Technology (NIST)-traceable thermometer immersed in the freezer until the time of analysis. Plasma and serum from the participants were analysed in batches of fifty after all samples have been collected.

Laboratory Analysis of Biochemical Parameters

Total cholesterol, Triglyceride and High density lipoprotein cholesterol were determined using the commercial kit (Randox)[®]. Low density lipoprotein Cholesterol was calculated using Friedewald Equation:

$$\text{LDL cholesterol (mmol/L)} = \text{Total cholesterol} - \text{HDL cholesterol} - \text{Triglyceride}/2.2$$

Data Analysis

Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0. Continuous data were presented as mean \pm (2) standard deviation and categorical

variables were presented as percentages. Statistical significance was taken as $p < 0.05$, and the confidence level set at 95%.

Ethical Clearance

Approval by the Ethical Review Committee of Ladoke Akintola University Teaching Hospital (LTH), Ogbomosho was obtained prior to the commencement of the study.

RESULTS

The study included 196 subjects consisting of 96 pregnant women across all the gestational age stratified into the three trimesters of pregnancy and 100 controls. The mean gestational age of subjects in the first trimester was (10 \pm 2) weeks; second trimester was (24 \pm 3 weeks) and third trimester was (34 \pm 3) weeks.

The weights of the pregnant women were significantly higher than that of the control (64.9 \pm 11.8 vs. 59.7 \pm 12.0kg, $p=0.01$). The body mass indexes were significantly higher among pregnant women than in the controls (26.0 \pm 4.1 vs. 23.2 \pm 4.4, $p< 0.001$). There was no difference in the body surface area between the two groups. (Table 1).

The mean total cholesterol (6.26 \pm 1.44 vs. 4.44 \pm 1.01 mmol/L, $P=0.001$), LDL-c (4.54 \pm 1.40 vs. 3.21 \pm 0.87 mmol/L, $p=0.010$) and Triglycerides (1.26 \pm 0.47 vs. 0.52 \pm 0.27 mmol/L, $p<0.001$) were significantly higher than that of the control. Additionally, the triglyceride in the controls demonstrated a value close to the lower limit of normal. (Table 2)

The increase in the total cholesterol and LDL-c were particularly higher in the third trimester and values were more than the reference range for normal individuals. The increase in the triglycerides was more in the first trimester with only modest increase in the second and third trimester with all the values within normal limits. (Fig. 1)

Table 1: Socio-demographic and Anthropometric Parameters of subjects and Controls

Variable	Subjects Mean \pm SD (n = 96)	Controls Mean \pm SD (n = 100)	P-value
Age (years)	28.1 \pm 5.1	26.4 \pm 5.3	0.10
Weight (kg)	64.9 \pm 11.8	59.7 \pm 12.0	0.010*
Height (m)	1.58 \pm 0.06	1.61 \pm 0.06	0.003*
BMI (g/m ²)	26.0 \pm 4.1	23.2 \pm 4.4	< 0.001*
BSA (m ²)	1.68 \pm 0.17	1.63 \pm 0.17	0.093
Average income (Naira)	14,940 \pm 18,792	13,401 \pm 8,248	0.566
Parity (N)			
0	35 (36.5%)	84 (84.0%)	
1	29 (20.2%)	6 (6%)	
2	14 (14.6%)	2 (2%)	
3	10 (10.4%)	5 (5%)	
4	7 (7.3%)	2 (2%)	
5	1 (1.0%)	1 (1%)	

Key: BMI= Body mass index, BSA= Body surface area, * statistically significant

Table 2: Lipid Profile pattern of subjects and control

Variables	Subjects (N=96) Mean \pm SD	Controls (N=100) Mean \pm SD	P-value
T chol (mmol/L)	6.26 \pm 1.44	4.44 \pm 1.01	0.001*
HDL-c (mmol/L)	1.17 \pm 0.37	1.02 \pm 0.17	0.065
LDL-c (mmol/L)	4.54 \pm 1.40	3.21 \pm 0.87	0.010*
Trig (mmol/L)	1.26 \pm 0.47	0.52 \pm 0.27	<0.001*
AIP	6.06 \pm 3.58	4.37 \pm 1.07	<0.001*

T.chol= total cholesterol, HDL-c= High density lipoprotein, LDL-c = low density lipoprotein. Trig= Triglyceride. * Statistical significance between all pregnant women and controls.

All the parameters in the lipid profile were higher in pregnant women but in a different pattern. The total cholesterol (T.chol), low-density lipoprotein cholesterol (LDL-c) and

triglyceride increased progressively from the first to the third trimester while the high-density lipoprotein cholesterol (HDL-c) demonstrated an initial increase in the first trimester with a fall towards the control value in the second trimester before a final rise in the third trimester. (Fig. 1)

DISCUSSION

The mean age was similar between the pregnant women and controls. The age at first pregnancy was higher in the controls possibly because more of them had tertiary education which was likely to have delayed their marriages and hence child deliveries. The mean weight and body mass index (BMI) of pregnant women were significantly

higher than those of the controls. This is expected due to the additional impact of the increase in the mass of the uterus, the fetus, amniotic fluid and placenta.

The pattern of lipid profile in pregnancy is such that it is influenced by changes which start occurring just after conception and keeps on evolving throughout the pregnancy till just after delivery. These changes occur in order to facilitate the needs of the mother and foetus. Therefore, as observed in our findings, there is a significant increase over that of control subjects in T.chol, LDL-c and triglyceride demonstrating a progressive increase from the first trimester through to the third trimester, while HDL-c demonstrated an initial increase in the first trimester with a subsequent fall in the second trimester before an eventual increase in the third trimester. This pattern is similar to a report from Idonije *et al* who studied 160 pregnant women of south southern Nigerian origin and reported a progressive rise in T.chol, LDL-c and triglyceride but low HDL-c pattern as demonstrated in this study.⁷ Butte however reported an initial decrease in the T.chol and LDL-c concentrations in the first trimester, followed by an increase in the second and third trimesters.⁹

Udoh *et al.* found a progressive increase in HDL-c as well as other parameters, T.chol,

LDL-c and Trig similar to other reports from authors like Adegoke who studied 120 pregnant women in southwestern Nigerian and Takahasha *et al* both of whom found a progressive increase in all the lipid parameters measured.¹⁰⁻¹² Almost all these studies reported a two-to-three-fold increase in triglycerides which was also demonstrated in this study. The large rise in triglycerides could be due to increased hepatic lipase activity enhancing hepatic triglyceride synthesis and reduction in lipoprotein lipase activity which results in decreased catabolism of adipose tissue.¹³

High triglyceride concentrations are used for maternal metabolic needs while reserving glucose for the fetus. The placental synthesis of steroids is facilitated by elevated LDL cholesterol levels. The second trimester is characterized by the accumulation of fat, which is later consumed by the mother in the third trimester. The association between elevated lipid levels during normal pregnancy and the development of atherosclerosis later in life has not yet been found. But it has been observed that the fall in HDL levels in the third trimester of a normal pregnancy could be a potential risk factor for developing atherosclerosis.¹⁴ Studies attempting to correlate the risk of coronary heart disease and the number of pregnancies have produced contradictory results.¹⁵

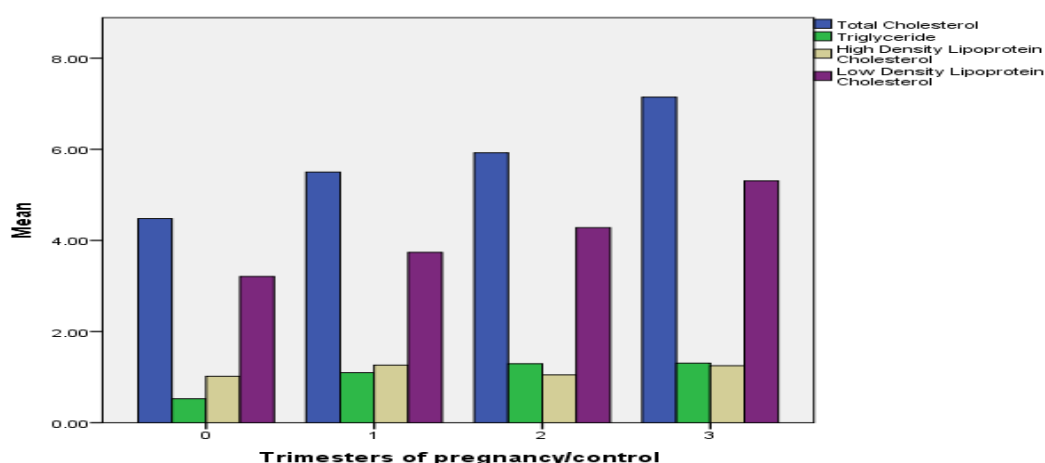


Figure 1: Bar chart showing the variation in the lipid profile in various trimesters of pregnancy. 0=controls, 1=subjects in first trimester, 2=subjects in second trimester, 3=subjects in second trimester.

Furthermore, studies have found that elevated TG levels lead to vascular

endothelial dysfunction and enhanced lipid peroxidation which resulted in damage to vascular endothelial cells. In a normal pregnancy, the level of antioxidant system activity increases at the same time to resist lipid peroxidation, and endothelium-dependent relaxation is enhanced in order to protect the pregnant women's cardiovascular system during pregnancy.¹⁶

Moreover, HDL-C is also protective of vascular endothelial cells by removing fat from tissues. As a result, abnormal lipid peroxidation will not appear in a normal pregnancy.¹⁶ Apart from this, in the highest gestational weight gain strata especially the third trimester, the effect of high-density lipoprotein cholesterol levels on the risk for small-for-gestational-age is larger. Elevated high-density lipoprotein cholesterol level during the third trimester could be considered as an indicator of a high risk of small-for-gestational-age, regardless of gestational weight gain.¹⁶ However, more research is needed in this area to establish the reports.

CONCLUSION

In accordance with other similar studies, the lipid profile parameters have been found to increase during pregnancy as demonstrated by our study. However, there is a need to further explore the clinical correlations of this increase with other systems especially, the cardiovascular system, in which this transient increase could be a risk factor for development of atherosclerosis or exacerbation of a preexisting cardiovascular disease condition among pregnant women.

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