ORIGINAL PROF-703

PREGNANCY RELATED HYPERLIPIDEMIA

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ABSTRACT

Objective: Changes are observed in the levels of very low density by operation, low density lipoprotein-cholesterol, and high density lipoprotein-cholesterol during pregnancy have been described. In the present study changes in lipids and lipoproteins have been investigated throughout the pregnancy and in the puerperium. Relationship between plasma lipids and other pregnancy related factors was studied. Data Source: Plasma levels of cholesterol, triglycerides and lipoproteins were determined in 56 pregnant women and the same number of non-pregnant women served as control. Study Design: Non interventional prospective: Setting: Department of Physiology, Quaid-e-Azam Medical College Bahawalpur. Period: August 1991 to August 2002. Material & Method: Fifty six (56) volunteer subjects in the first trimester of pregnancy were chosen from those attending routine antenatal out patient department of various hospitals of Bahawalpur. Results: The plasma concentrations of cholesterol, triglycerides and lipoproteins increased significantly during the second trimester and reached maximum in the third trimester. Furthermore, total cholesterol and total triglycerides, contents in different fractions lipoproteins, decreased significantly higher until 4 weeks of post-partum. The magnitude of the cholesterol increment appeared in part to be related to that of serum triglycerides but was independent of age, weight gain, numbers of previous pregnancies and sex of the foetus. Conclusion: It is conceivable, therefore, that hyperlipidemia does occur during pregnancy in women.

KEY WORDS: Lipoproteins, plasma lipids, pregnancy, puerperium.

INTRODUCTION

It has been reported that increased levels of serum total cholesterol, specially the low density lipoproteins, are a major risk factor for cardiovascular diseases[1,2]. In Western populations, normal pregnancy leads to an increase in cholesterol by approximately 25%, while the triglycerides level increases twofold to threefold[3-4]. Changes in lipoproteins composition have also been reported in both lipid and protein moieties. However, in Pakistani women, these changes have not been reported. Moreover, previous studies have concentrated on the last trimester of pregnancy. In the present study longitudinal changes in the concentrations of plasma cholesterol and triglycerides and their distribution among the lipoprotein fractions of plasma during the whole course of pregnancy and in the puerperium have been described. In addition, efforts were made to study the relationship between plasma lipids and other factors such as age, weight gain, diet, numbers of previous pregnancies and sex of the foetus.

MATERIAL & METHODS

All experimental procedures adhered to the Declaration of Helsinki of the World Medical Association. The work was approved by the Ethics Committee of the institution and subjects gave informal consent to participate in the study. Fifty-six (56) volunteer subjects in the first trimester of pregnancy were chosen from those attending routine antenatal out-patient department of various hospitals of Bahawalpur. The same number of controls were taken from the nurses and other working staff of the same hospital. Of the control subjects, no one was using contraceptives. For all pregnant women, the date of the last menstrual period (LMP) was accurately known. All participants were of the same age group, ranging between 21 and 25 years. All demographic factors of the groups were also comparable. All of these subjects met the following conditions of health;

1). They were not under medical treatment;
2). They did not have any history of cardiac or hepatobiliary disease, and who had no abnormal subjective symptoms;
1) Lastly who did not exhibit abnormalities such as in blood pressure on routine physical examinations.

Records of the age, parity, of both pregnant and non-pregnant groups were made. Blood samples were taken monthly throughout the pregnancy, at the time of delivery, within 12 to 24 hours of delivery (designated Day 1) and on the sixth day post-partum. Following discharge from the hospital, further samples were taken every four weeks until the 20^{th} post partum week. Plasma lipids and lipoproteins lipid values were also obtained for non-pregnant control women. The subjects were advised to fast overnight 12-16 hours before the test and were directed not to do any exercise and fasting was confirmed by carefully questioning the participants at the time of their test; any non-fasting individuals were rescheduled. Brachial blood pressure measurements were taken with a calibrated sphygmomanometer in sitting position after a complete rest of 15 minutes in supine posture. Venous blood was drawn into Vacutainer tubes containing 1 mg per ml desodium EDTA, plasma was separated within 2 hour and kept at 4^0C. Plasma lipoproteins were separated into very low density (VLDL, having density less than 1.006 grams per liter), and high density (HDL having a density between 1.063 and 1.21 grams per liter lipoproteins. VLDL's were isolated by preparative ultracentrifugation[5] and LDL's were precipitated with heparin sulphate and manganese chloride[6]. Lipids were extracted into isopropanol-hepatane. The laboratory procedures were standardized according to the criteria for the Lipid Research Clinics[7]. Concentrations of plasma cholesterol and triglycerides, VLDL, LDL and HDL were determined using the procedures of the Lipid Research Clinic(7). The analysis were performed on an Auto Analyzer II. Mean recoveries of lipoprotein cholesterol and triglycerides were 93 and 95%, respectively.

RESULTS

Out of fifty six (56) pregnant women, no one had any complications. Blood pressure of all the subjects remained within the normal range. Of the babies, 31 were male and 25 female and all were healthy, within a weight range of 2.41-3.98 kg. All babies were breast-fed from birth for a period lasting from 16 to 42 weeks. From the replies to the initial diet questionnaire, none disclosed any consistent trend in the variation of eating habits sufficient to be the primary cause of the large biochemical variations observed. The duration of pregnancy was 35-40 weeks. The magnitude of plasma cholesterol increment appeared in part to be related to that of plasma triglycerides, but no other significant correlating factor was found and they appeared to be independent of age, weight gain, diet, numbers of previous pregnancies and sex of the foetus. There were marked variations among individuals in the extent of increase in both cholesterol and triglycerides. Changes in the concentrations of total cholesterol and triglyceride are displayed in Table-I. Similarly the changes in cholesterol and triglyceride components of lipoproteins are given in Table-I. Compared to control group, concentrations of cholesterol and triglycerides of plasma VLDL, LDL were slightly and non-significantly higher ($p>0.5$) during first trimester. Total triglycerides and cholesterol concentrations of total plasma VLDL, LDL and HDL were all significantly increased during the second trimester and reached maximum in the third trimester of pregnancy. Both cholesterol and triglyceride concentrations decreased significantly within 24 hours of delivery and this was reflected in all lipoproteins. In the majority of subjects, cholesterol and triglycerides remained high until the 4^{th} week post-partum. These findings have suggested that hyperlipidemia is common during pregnancy in Bahawalpur.

DISCUSSION

The main finding of the present study was an increase in cholesterol and triglycerides of total plasma VLDL, LDL, and HDL during pregnancy. This result is consistent with many other studies conducted in Western countries[3,4,9,13]. Changes in plasma lipids during pregnancy observed in this study are comparable with the changes reported in Western countries[10,13].

Table-I. Plasma lipids and lipoprotein changes during pregnancy and in the puerperium

Duration (Weeks)	VLDL		LDL		HDL	
	Cholesterol	Triglycerides	Cholesterol	Triglycerides	Cholesterol	Triglycerides
Control	0.22 0.01	0.49 0.08	3.21 0.09	0.32 0.04	1.51 0.11	0.27 0.05
4	0.25 0.04	0.43 0.07	3.22 0.15	0.36 0.03	1.57 0.13	0.26 0.03
8	0.25 0.03	0.40 0.10	3.42 0.10	0.44 0.11	1.77 0.16	0.32 0.07
12	0.28 0.06	0.59 0.14	3.80 0.17	0.59 0.17	1.89 0.12	0.40 0.11
16	0.37 0.06	0.92 0.16	4.02 0.29	0.70 0.80**	2.22 0.19	0.52 0.05**
20	0.42 0.10*	0.93 0.03***	4.04 0.37	0.88 0.05**	2.22 0.19*	0.52 0.05***
24	0.47 0.11*	0.96 0.15***	4.54 0.31****	0.93 0.07**	2.26 0.11*	0.53 0.03**
28	0.97 0.12**	1.34 0.13**	4.81 0.23**	1.21 0.11**	2.01 0.21*	0.52 0.02**
32	0.99 0.11**	1.49 0.12**	4.87 0.29**	1.29 0.13**	2.04 0.19*	0.55 0.04**
36	1.04 0.13**	1.71 0.09**	4.99 0.27**	1.37 0.10**	1.99 0.03*	0.56 0.07**
Delivery	1.05 0.12**	1.77 0.15**	5.49 0.47**	1.44 0.16**	1.97 0.07*	0.51 0.06**
Day 1	0.99 0.13**	1.71 0.13**	5.01 0.36**	0.84 0.18*	2.01 0.09*	0.59 0.14**
Day 6	0.83 0.17**	1.51 0.19**	4.66 0.31**	0.67 0.19	2.07 0.11*	0.45 0.11*
Week 4	0.71 0.14**	1.08 0.11**	4.67 0.39**	0.66 0.16	1.79 0.12	0.6 0.06*
Week 8	0.45 0.11*	0.66 0.19	4.06 0.42	0.59 0.28	1.80 0.16	0.39 0.19
Week 12	120.29 0.09	0.54 0.17	3.41 0.29	0.41 0.24	1.72 0.09	0.32 0.22
Week 16	160.27 0.08	0.52 0.15	3.39 0.47	0.41 0.18	1.71 0.07	0.29 0.11
Week 20	200.28 0.10	0.52 0.11	3.38 0.49	0.40 0.10	1.69 0.11	0.26 0.06

Values mmol/liter expressed as mean SEM
*Differences are significant (*p<o.o5; **p<0.001; ***p<0.02; p<0.01 as compared to control group*

This physiologic hyperlipidemia is potentially significant in several points; first, the increase in plasma triglycerides may enhance the availability of essential and nonessential triglyceride fatty acids for placental transfer to the foetus[14]; second, the blood cholesterol rise, may increase the supply of cholesterol needed for placental progesterone synthesis[15] and transplacental cholesterol transfer to the foetus[16]; and third, the hyperlipidemia of pregnancy could itself function as an arteriosclerosis risk factor[17].

The physiological significance of these changes could be related to the initiation and maintenance of lactation. After delivery, the elevated serum triglyceride concentrations decreased rapidly, the significantly greater utilization of serum triglycerides in lactating women could be caused by the tissue-specific direction of VLDL towards the mammary glands for milk synthesis. Evidence to support this hypothesis is provided by studies of post-partum rats[18]. Lipoprotein lipase activity is depressed in adipose tissue but greatly elevated in mammary glands. After delivery, lipids and lipoproteined levels start to decrease but remained significantly higher until the fourth week, except VLDL cholesterol which remained high until the eight week. The persistent elevation of both cholesterol and triglyceride levels six to seven weeks post-partum, has been previously demonstrated[3,18]. This hyperlipidemia may be hormonally mediated. For instance, altered triglyceride kinetics may be detected up to six weeks after ending the use of oral contraceptives[19]. While many physiologic parameters apparently return to normal soon after removal of the foetus and placenta (for instance, there is an immediate improvement in the hypertension associated with pre-eclampsia), restoration of other metabolic functions accompanying the return of hormonal equilibrium may take much longer.

The physiological mechanisms responsible for the increase in cholesterol and triglycerides during pregnancy are not clearly known[9,13]. A number of possible mechanisms can be postulated. Corredor et al[20] reported that plasma cholesterol and triglyceride concentrations were positively correlated with estradiol-17β, progesterone, human placental lactogen levels throughout the whole period of gestation. The hypercholesterolemia during pregnancy may be related to the increased production of sex steriord[21,22]. In experimental animals, the activity of lipoprotein lipase enzymes had been shown to decrease during pregnancy[23]. These changes are specific for the adipose tissue enzyme as lipoprotein lipase activity in heart, lung, diaphragm and mammary glands is unaffected[24]. The decrease of lipoprotein lipase activity in adipose tissue could explain the increase in plasma lipids and lipoproteins during pregnancy.

Idea that hyperlipidemia of pregnancy is itself an arteriosclerosis-promoting event has been debated in previous studies[3,4,17,21] but is without conclusive proof, which is perhaps not surprising because of the present observations. Obviously, more work is required to determine the extent to which changes in lipoprotein physiology in pregnancy bear on the risk of arteriosclerosis.

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There must be more to life than having every thing.

Maurice Sendak