ELSEVIER

Atherosclerosis 162 (2002) 425–432

ATHEROSCLEROSIS

www.elsevier.com/locate/atherosclerosis

Changes in LDL size and HDL concentration in normal and preeclamptic pregnancies

Luís Belo [a,b,*], Muriel Caslake [c], Dairena Gaffney [c], Alice Santos-Silva [a,b], Luís Pereira-Leite [d], Alexandre Quintanilha [b,e], Irene Rebelo [a,b]

[a] *Department of Biochemistry, Faculty of Pharmacy, University of Porto, Rua Anibal Cunha 164, 4050-047 Porto, Portugal*
[b] *Institute for Molecular and Cell Biology, University of Porto, 4150-180 Porto, Portugal*
[c] *Department of Pathological Biochemistry, Glasgow Royal Infirmary, University N.H.S. Trust, G31 2ER Glasgow, UK*
[d] *Department of Obstetrics and Gynaecology, Porto Medical School, Hospital of S. João, 4200-319 Porto, Portugal*
[e] *Institute of Biomedical Sciences of Abel Salazar, University of Porto, 4099-003 Porto, Portugal*

Received 12 April 2001; received in revised form 14 September 2001; accepted 28 September 2001

Abstract

The aim of this study was to evaluate changes in lipids, apolipoproteins and lipoproteins in Portuguese pregnant women and their potential involvement in the pathophysiology of preeclampsia. A cross-sectional study was performed by collecting blood samples in the first ($n = 64$), second ($n = 48$) and third ($n = 67$) trimesters and *puerperium* ($n = 32$) of normal pregnancies. Samples from preeclamptic women were obtained in the third trimester ($n = 51$) and in *puerperium* ($n = 26$). As normal pregnancy progressed and triglyceride (TG) levels rose there was a decrease in low density lipoprotein (LDL) size, as measured by peak and mean particle diameter (MPD), with an increased proportion of atherogenic small dense LDL. Preeclamptic women exhibited, in the third trimester and *puerperium*, higher mean serum TG concentration and lower high density lipoprotein (HDL) cholesterol and apolipoprotein A-I (apo A-I) levels compared with healthy pregnant women. In the third trimester, LDL–mean particle diameter (LDL–MPD) and LDL cholesterol–apolipoprotein B (LDLc–apo B) ratio were also significantly reduced in the pathologic group. We conclude that human gestation is associated with an 'atherogenic' lipid profile that is further enhanced in preeclampsia and that this profile may be a potential contributor to endothelial cell dysfunction.

Keywords: LDL size; HDL concentration; Normal pregnancy; Preeclampsia

1. Introduction

Preeclampsia is a characteristic multisystem disorder of pregnancy and is a leading cause of maternal and perinatal morbidity and mortality [1]. The typical pattern in the uteroplacental bed of this pathology is acute atherosis of decidual vessels [2]. Endothelial cell dysfunction may play a pivotal role in the genesis of the multisystem damage developed in preeclampsia. Causes for endothelial dysfunction in this disorder have been suggested but are still controversial [3].

Hyperlipidaemia can compromise endothelial function and this may contribute to the development of atherosclerotic vascular disease [4]. Human pregnancy is associated with pronounced physiological hyperlipidaemia [5]. In normal pregnancy this feature is not atherogenic and is believed to be under hormonal control [6]. In complicated pregnancies the mechanisms regulating physiologic hyperlipidaemia may malfunction. Abnormal lipid profiles and species may have a role in the promotion of oxidative stress and vascular dysfunction seen in preeclampsia [7].

The normal gestational increase in triglycerides (TG) is associated with a change in low density lipoprotein (LDL) profile towards smaller denser species [8], and is further increased in preeclampsia [9]. In agreement with this, LDL–peak particle diameter (LDL–PPD) is sig-

* Corresponding author. Tel.: +351-22-207-8906; fax: +351-22-200-3977.
E-mail address: luis_fbelo@yahoo.com (L. Belo).

0021-9150/02/$ - see front matter
PII: S0021-9150(01)00734-1

nificantly decreased in preeclampsia relatively to normal pregnancy [10]. We suggest it would be important to measure not only LDL–PPD (predominant LDL size at maximum optical density) but also LDL–mean particle diameter (LDL–MPD), a reliable indicator of the size of the entire LDL population. The evaluation of LDL size is important because smaller, denser subpopulations of LDL are more susceptible to oxidation [11]. Once oxidised, LDL is believed to have enhanced atherogenic potential, promoting foam cell formation and initiating endothelial dysfunction [11]. On the other hand, high density lipoprotein (HDL) has a protective role in the development of atherosclerosis [12]. Whereas, there is a strong inverse relationship between HDL cholesterol (HDLc) concentration and atherogenic situations [13] no agreement exists in literature about changes in HDLc in preeclamptic pregnancies. Moreover, recent observations [14] have demonstrated the potential anti-inflammatory action of HDL which highlight the importance of measuring this parameter.

The aim of our work was to evaluate changes in lipid profile in Portuguese women during normal pregnancy and the eventual role of these changes in the pathophysiology of preeclampsia. Lipid profile included the evaluation of total cholesterol (Chol), TG, apolipoprotein A-I (apo A-I), apolipoprotein B (apo B), HDLc, LDL cholesterol (LDLc), LDL–MPD, LDL–PPD and its relative proportion of 3 subfractions. Chol–HDLc, LDLc–apo B and HDLc–apo A-I ratios were also calculated.

2. Material and methods

2.1. Subjects

All women were admitted between December 1998 and February 2000 to the Obstetrical Service of University Hospital S. João, Porto, Portugal. Patients were asked to participate in this study following a protocol approved by the Committee on Ethics of the University Hospital S. João.

Normal pregnancy was diagnosed on the basis of clinical and ultrasound findings. Healthy pregnant women had a normal course and outcome of pregnancy and did not receive any medication known to interfere with lipid metabolism. Diagnosis of preeclampsia was determined by gestational hypertension accompanied by proteinuria, oedema, or both. In agreement with the Committee on Terminology of the American College of Obstetricians and Gynecologists, gestational hypertension was defined as an increase by at least 30 mmHg systolic or 15 mmHg diastolic blood pressure compared with values obtained before 20 weeks of gestation, or a sustained blood pressure of at least 140/90 mmHg after 20 weeks, if prior blood pressure was not known. Proteinuria was defined as the excretion of 300 mg of protein or greater in a 24 h urine collection specimen. This usually correlates with 30 mg/dl (1 + on dipstick testing) or greater in a random urine determination. Since proteinuria may be confounded with infection, routine cytobacteriologic exams and sequential urinary sediments were performed in all preeclamptic women to exclude that possibility. Oedema was diagnosed as clinically evident swelling or as a rapid increase of weight. Preeclamptic women received anti-hypertensive therapy and low salt diet. All patients with significant obstetric disease other than preeclampsia or nonpregnant related complications/habits were eliminated from the study. Clinical data regarding the sample population was collected. A cross-sectional study was performed using 288 pregnant women. Blood samples were collected in the first ($n = 64$), second ($n = 48$) and third ($n = 67$) trimesters and *puerperium* ($n = 32$) of normal pregnancy. We also studied preeclamptic women in the third trimester ($n = 51$) and in *puerperium* ($n = 26$).

2.2. Blood samples

Non-fasted blood samples obtained during pregnancy and in *puerperium* (24–48 h *post-partum*), were processed within 2 h of collection. Blood was obtained by venipuncture in sterile tubes containing dipotassium ethylenediaminetetraacetic acid (EDTA) and in test tubes without anticoagulant. After centrifugation, plasma was taken from the EDTA containing tubes and serum from the tubes in which blood was allowed to coagulate. Aliquots were immediately stored at -70 °C until assayed.

2.3. Serum analysis

Serum lipids, lipoproteins and apolipoproteins analysis were performed in an auto-analyser (Cobas Mira S, Roche) using commercially available kits. Serum Chol and TG concentrations were determined by enzymatic colorimetric tests (CHOD-PAP and GPO-PAP methods, Roche, respectively). HDLc and LDLc levels were measured using enzymatic colorimetric tests after selective separation of HDL and LDL fractions (Direct HDL-Cholesterol and Direct LDL-Cholesterol, Roche). Apo A-I and apo B levels in serum were evaluated by immunoturbidimetric assays (uni-kit apo A-I and B specific antiserums, Roche).

2.4. Plasma analysis

LDL at d1.019–1.063 g/ml was isolated from plasma. Electrophoresis was carried out, as described

elsewhere [15]. We used 2–16% polyacrylamide gels (Alamo Gels, San Antonio, TX) to determine LDL–PPD, LDL–MPD and the relative proportions of LDL I, LDL II and LDL III. The gels were standardised against three samples prepared by density gradient ultracentrifugation with different LDL–PPD (LDL I, II and III) which had previously been calibrated against markers, Seradyn latex (38 nm), Thyroglobulin (17 nm) and Ferritin (12.20 nm). The gels were scanned by laser densitometry (Bio-Rad Multi-Analyst™/PC Version 1.1). LDL–PPD was reported as the size of the major LDL fraction. LDL–MPD was calculated to give the mean diameter across the entire LDL profile. To achieve this, each peak of the LDL profile was sliced into ten portions and the peak area under the curve (volume) was calculated. For each portion, the particle size was calculated using the known reference sizes of LDL I, II and III. Then, the frequency for each particle was calculated (size × volume). Finally, the sum of frequencies divided by the sum of volumes gave the MPD.

2.5. Statistics

Kolmogorov–Smirnov analysis was used to test if the results are normally distributed. In normal pregnancy, multiple comparisons between groups were performed by one-way analysis of variance (ANOVA) supplemented with Tukey's HSD post hoc test. Preeclamptic and control patients were compared using Student's unpaired t-test and adjustment of statistical differences for confounding factors was performed using analysis of covariance (ANCOVA). Correlations between parameters were evaluated by calculating the Pearson correlation coefficient (r). Significance was accepted at $P < 0.05$.

3. Results

3.1. Clinical data

Tables 1 and 2 summarise the clinical characteristics of all patients. Mean age did not differ between all groups. As mean gestational age increased, during the course of normal pregnancy, there was a rise in weight and uric acid level. No major changes were seen in the blood pressure for the same period. In the third trimester, preeclamptic women presented higher mean weight and uric acid level compared with control pregnant women. They also presented with proteinuria and higher systolic and diastolic blood pressure. Gestational age at delivery, infant birth weight and Apgar scores were smaller for preeclamptic women. Uric acid was also significantly elevated in the pathologic *puerperium*.

3.2. Lipids and lipoproteins

Fig. 1(A) shows an example of a LDL band profile, by densitometry analysis, indicating the corresponding LDL mean and peak particle diameters as well as the relative proportion of LDL I, II and III. Table 3 presents lipids and lipoproteins during normal pregnancy and *puerperium*. There was a significant rise in serum levels of TG, Chol, apo B, apo A-I, HDLc and LDLc from the first to the second trimester of normal pregnancy and a further increase in TG, Chol, apo B and LDLc in the third trimester with a decrease in HDLc and apo A-I. Except for TG concentration, all these parameters decreased significantly in *puerperium*. As pregnancy progressed from first to second trimester the MPD and PPD became significantly smaller, with no further decrease in size in the third trimester. There was a significant increase in proportion of LDL III between first and third trimesters (30–37%, $P < 0.01$).

Table 1
Clinical characteristics of patient groups in pregnancy

	Normal			Preeclamptic	P
	First trimester ($n = 64$)	Second trimester ($n = 48$)	Third trimester ($n = 67$)	Third trimester ($n = 51$)	
Age (years)	27.7 ± 5.3	26.3 ± 6.3	26.2 ± 4.8	28.0 ± 5.5	NS
Gestational age (weeks)	10.1 ± 2.0	22.3 ± 2.8	34.0 ± 2.8	34.4 ± 3.6	NS
Weight (kg)	62.1 ± 9.2	67.1 ± 9.6	73.9 ± 9.9	80.1 ± 14.8	<0.05
Uric acid (mg/dl)	2.9 ± 0.7	3.2 ± 0.9	4.0 ± 1.1	6.5 ± 1.8	<0.001
Blood pressure (mmHg)					
Systolic	115 ± 13	118 ± 11	119 ± 11	152 ± 12	<0.001
Diastolic	59 ± 10	58 ± 10	62 ± 9	92 ± 9	<0.001
Proteinuria (+)	n.d.	n.d.	n.d.	2 ± 1	<0.001

Values are given as mean ± S.D.; n.d., non detectable; P values present the differences in the third trimester between normal and preeclamptic pregnancies.

Table 2
Clinical characteristics of patient groups in *puerperium*

	Normal ($n = 32$)	Preeclamptic ($n = 26$)	P
Age (years)	25.5 ± 3.3	27.5 ± 5.3	NS
Gestational age at delivery (weeks)	38.8 ± 1.1	36.2 ± 2.6	<0.001
Uric acid (mg/dl)	5.0 ± 1.1	6.8 ± 1.8	<0.001
Infant birth weight (kg)	3.29 ± 0.37	2.57 ± 0.78	<0.001
Apgar score			
One min	8.4 ± 1.0	7.1 ± 1.8	<0.01
Five min	9.8 ± 0.4	9.0 ± 1.2	<0.01

Values are given as mean $\pm$ S.D.

This is demonstrated in Fig. 1(B) that shows the appearance of low particle size bands, corresponding to smaller denser LDL, as pregnancy advances. Chol–HDLc and LDLc–apo B ratios increased as pregnancy progressed and decreased after delivery. Inverse behaviour was observed in the HDLc–apoA-I ratio.

Preeclamptic women, in the third trimester and *puerperium*, exhibited higher mean serum TG concentration and lower HDLc and apo A–I levels compared with healthy pregnant women (Table 4). In the third trimester, LDL–MPD and LDLc–apo B ratio were also significantly reduced in the pathologic group. All the differences between normal and preeclamptic pregnancies remained significant after adjustment for weight of the mothers. The effect of delivery on lipid parameters was not so pronounced in preeclampsia, with small significant reductions observed only in Chol, apo A–I, HDLc and LDLc–apo B ratio (Table 4).

3.3. Association of lipid parameters

Using all results of the cross-sectional study (288 samples), a significant inverse correlation was obtained between TG and LDL–MPD ($r = -0.360$, $P < 0.001$). TG versus LDL–PPD presented a similar association ($r = -0.372$, $P < 0.001$).

LDLc–apo B ratio also correlated positively with LDL–MPD ($r = 0.145$, $P < 0.05$) and inversely with the relative proportion of LDL III ($r = -0.125$, $P < 0.05$).

4. Discussion

Patients with preeclampsia were generally admitted on an emergency basis. As a consequence, anti-hypertensive therapy had been started in some cases before a blood sample could be obtained. Anti-hypertensives are known to modify lipid and lipoprotein concentrations. However, in pre-treated cases, drugs were administered for only few hours. Therefore, we assume that these drugs had no marked effect on the evaluated parameters. Also, as standardised blood sampling after a 12 h overnight fast was not feasible in a study involving emergency cases, samples were collected on a non-fasting basis. Postprandial serum lipid and lipoprotein levels seem to have no substantial short-term effects, except for TG concentration [16]. There is also some evidence that fasting status has no significant effect on LDL particle diameter [10]. This was also confirmed in this study since non-fasting TG correlated significantly with both LDL–MPD and PPD.

The observed significant rise in lipid levels during the human gestation in this experiment is in agreement with previous studies [5,6]. We also confirmed changes in the level and composition of lipoproteins. Hormonal influence seems an attractive explanation for the lipid changes in pregnancy [6]. Despite major lipid modifications in normal pregnancy, this phenomenon is well tolerated by the mother. It also seems to be related to the need of supplying the growing foetus with metabolic precursors, such as cholesterol and TG.

Serum LDL is not an homogeneous entity; it contains discrete particles varying in size, density, composition and function. Larger more buoyant LDL particles (LDL I and II) are distinct from small, dense LDL (LDL III). Smaller, denser LDL particles are known to be more atherogenic: they exhibit reduced receptor binding and are more susceptible to oxidation [11]. Oxidised LDL is believed to be highly atherogenic, promoting foam cell formation and initiating endothelial dysfunction [11]. Oxidised LDL particles also impair endothelial-dependent vascular relaxation [17]. It is speculated [18] that the presence of different types of LDL particles is a function of multiple pathways of lipoprotein metabolism, and that atherogenicity is actually determined by LDL and a combination of other factors.

Our results show that as pregnancy progresses and TG levels rise there is a decrease in LDL size, corresponding to an increased proportion of atherogenic small dense LDL. We should refer that most of the reported studies in this field, were performed by using much smaller numbers.

This is the first report of LDL–MPD values in pregnancy. We believe that LDL–MPD is a more consistent indicator than LDL–PPD of the size of LDL

Table 3
Lipids and lipoproteins in normal pregnancy and *puerperium*

	First trimester ($n = 64$)	Second trimester ($n = 48$)	*P* first/second	Third trimester ($n = 67$)	*P* second/third	*P* first/third	*Puerperium* ($n = 32$)	*P* third/Puer
TG (mg/dl)	113.6 ± 40.6	147.7 ± 38.1	<0.001	185.8 ± 38.4	<0.001	<0.001	179.9 ± 24.4	NS
Chol (mg/dl)	176.0 ± 30.5	252.2 ± 46.9	<0.001	285.1 ± 63.6	<0.01	<0.001	219.2 ± 50.6	<0.001
Apo B (mg/dl)	77.0 ± 15.8	112.4 ± 24.4	<0.001	126.8 ± 31.0	<0.01	<0.001	107.2 ± 34.5	<0.01
Apo A–I (mg/dl)	171.8 ± 37.5	224.2 ± 29.0	<0.001	211.5 ± 47.5	NS	<0.001	184.8 ± 38.0	<0.01
HDLc (mg/dl)	54.8 ± 13.7	69.8 ± 12.7	<0.001	61.8 ± 14.2	<0.01	<0.01	55.2 ± 14.1	<0.05
LDLc (mg/dl)	84.0 ± 19.5	122.7 ± 31.0	<0.001	145.9 ± 44.5	<0.01	<0.001	107.6 ± 34.8	<0.001
LDL–MPD (nm)	26.66 ± 0.56	26.36 ± 0.46	<0.01	26.34 ± 0.52	NS	<0.01	26.23 ± 0.52	NS
LDL–PPD (nm)	26.60 ± 0.57	26.19 ± 0.55	<0.01	26.09 ± 0.63	NS	<0.001	26.14 ± 0.61	NS
LDL I (%)	22.66 ± 12.33	19.99 ± 9.68	NS	21.45 ± 8.78	NS	NS	18.23 ± 9.50	NS
LDL II (%)	46.80 ± 8.31	45.16 ± 6.23	NS	41.66 ± 7.44	<0.05	<0.001	47.44 ± 8.88	<0.01
LDL III (%)	30.54 ± 13.37	34.84 ± 11.27	NS	36.89 ± 12.94	NS	<0.05	34.33 ± 14.97	NS
Chol:HDLc	3.22 ± 0.60	3.65 ± 0.81	<0.05	4.62 ± 1.21	<0.001	<0.001	4.20 ± 1.36	NS
LDLc:Apo B	1.08 ± 0.15	1.09 ± 0.15	NS	1.14 ± 0.15	NS	NS	1.00 ± 0.17	<0.01
HDLc:Apo A–I	0.32 ± 0.05	0.31 ± 0.04	NS	0.29 ± 0.04	NS	<0.05	0.30 ± 0.04	NS

Values are given as mean ± S.D.

particles. While LDL–PPD indicates only the predominant LDL size at the major LDL band, LDL–MPD describes the size profile of the entire LDL population (all bands taken into account; see Fig. 1(A)). To address the same problem, some authors use the 'LDL particle score'. This score is a calculation that involves the contribution of the relative proportion of each of the LDL subfractions [19]. The higher the particle score, the smaller the particle size (the smaller the LDL–MPD). However, we think it makes more sense to use LDL–MPD, a real measure of particle size, to compare with LDL–PPD; as rather than giving an arbitrary number, the LDL–MPD value can be equated to LDL particle sizes that have been quoted in the literature over the last 20 years.

Hypertensive disorders of pregnancy are associated with increased TG levels [20]. It has also been observed [16] that TG levels in the LDL fraction are higher in pregnancy-induced hypertension patients compared with controls. Hypertriglyceridaemia in preeclampsia is proposed to include oxidant stress by promoting changes in the composition of LDL and consequently enhancing the formation of small dense LDL [9,10]. This is concordant with our findings. Our group of preeclamptic women showed, in the third trimester of gestation, significant higher levels of TG and lower LDL–MPD compared with pregnant controls.

LDL–MPD was indeed significantly reduced in the pathologic group, but not LDL–PPD. The significantly higher proportion of LDL II associated with a more homogeneous LDL population in the preeclamptic group was responsible for this. In fact, although LDL–PPD did not differ between groups, the LDL population seems to be more dispersed in the control group and, therefore, LDL–MPD is significantly higher.

Preeclamptic women also presented higher mean weight compared with matched controls and this could be a major confounder in all the lipid results. However, statistical differences were still present after adjustment for weight.

Concerning the analysis of the LDLc–apo B ratio, we must take into consideration the fact that apo B refers to serum apolipoprotein B concentration. Thus, although the reduced LDLc–apo B ratio in the preeclamptic group is in agreement with the reduction of the LDL diameter, the reduced ratio may also be due to an increase in other apo B containing lipoproteins. Very low density lipoprotein (VLDL), for instance, is likely to be increased in preeclampsia as TG level is much higher in this group.

In addition, in the preeclamptic group, we found significant low levels of HDLc and apo A–I, the major protein constituent of HDL. Again, this was still true after correction for weight. Some studies have already reported similar results in HDLc [9,21] and Apo A–I [21] levels but others [22,23] have failed to detect differences in HDLc. The lack of association in the latter two studies could be explained by the small numbers of subjects used. HDL is believed to have a protective function in atherosclerosis [12]. Its role in reverse cholesterol transport [13], in anti-oxidant [24], anti-aggregatory [25] and/or anti-inflammatory effects [14] are possibly related to its anti-atherogenic capacity. In human gestation, there is a rise in HDLc and apo A-I concentrations reaching a peak in the second trimester. The increase in the number of HDL particles may help to protect the mother, counterbalancing the 'atherogenic' modifications of the apo B containing lipoproteins during pregnancy. In preeclampsia, the reduced levels of HDLc and apo A-I seem to indicate an uncompensated protective state. It may reveal a failure of HDL to rise, during gestation, or simply naturally occurring lower levels of HDL in these women. In fact, HDLc and apoA-I concentrations were still significantly reduced in *puerperium* of preeclamptic women and were also lower than the values observed in the first trimester of normal pregnancy.

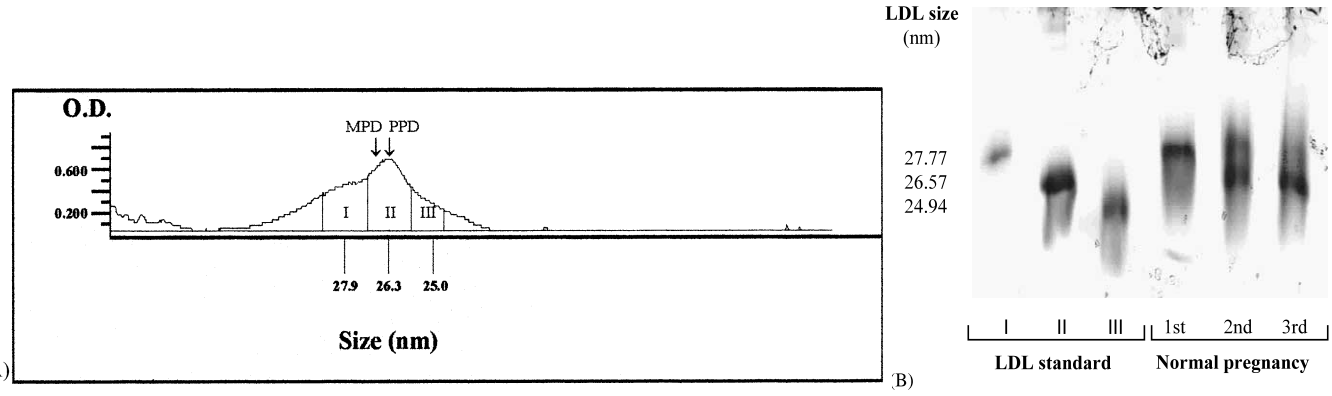

Fig. 1. (A) LDL band profile, of one sample, by densitometry analysis. The corresponding LDL mean (MPD) and peak (PPD) particle diameters are indicated as well as the relative proportion of LDL I–III. In this example, LDL II presents the major contribution; the relative proportion of LDL I is greater than LDL III and, therefore, MPD is higher than PPD. (B) LDL gel profile of three different samples in the first, second and third trimesters of normal pregnancy.

Table 4
Lipids and lipoproteins in third trimester and *puerperium* in preeclampsia

	Third trimester ($n = 51$)	*Puerperium* ($n = 26$)	*P* third/Puer	*N* vs. PE	
				P third/third	*P* Puer/Puer
TG (mg/dl)	238.8 ± 85.6	217.4 ± 70.6	NS	<0.001	<0.05
Chol (mg/dl)	268.2 ± 94.7	224.2 ± 65.0	<0.05	NS	NS
Apo B (mg/dl)	130.5 ± 50.6	121.1 ± 38.2	NS	NS	NS
Apo A-I (mg/dl)	188.5 ± 44.1	159.4 ± 35.0	<0.05	<0.01	<0.05
HDLc (mg/dl)	54.2 ± 14.5	48.0 ± 8.7	<0.05	<0.01	<0.05
LDLc (mg/dl)	140.3 ± 60.9	117.9 ± 46.7	NS	NS	NS
LDL–MPD (nm)	26.05 ± 0.59	26.22 ± 0.48	NS	<0.01	NS
LDL–PPD (nm)	25.95 ± 0.67	26.15 ± 0.55	NS	NS	NS
LDL I (%)	20.54 ± 10.32	21.52 ± 9.19	NS	NS	NS
LDL II (%)	46.11 ± 11.02	45.22 ± 10.04	NS	<0.05	NS
LDL III (%)	33.36 ± 18.47	33.26 ± 17.32	NS	NS	NS
Chol:HDLc	5.02 ± 1.86	4.54 ± 1.18	NS	NS	NS
LDLc:Apo B	1.05 ± 0.17	0.93 ± 0.20	<0.05	<0.01	NS
HDLc:Apo A-I	0.29 ± 0.05	0.31 ± 0.05	NS	NS	NS

Values are given as mean ± S.D.; *N* vs. PE, comparison between normal and preeclamptic pregnancies.

Atherogenicity is believed to be determined by a conjunction of factors [18]. We agree that in preeclampsia a combination of certain risk factors (increased small dense LDL and TG concentrations and reduced HDLc and apo A-I levels) may lead to the atherosclerotic process in decidual vessels.

We conclude that the atherogenic profile, well tolerated by the mother during normal pregnancy, might somehow disrupt the normal processes in the preeclamptic mother. Moreover, abnormal lipid profile may have a potential role in the promotion of oxidative stress and vascular dysfunction seen in preeclampsia.

Acknowledgements

The authors wish to thank Laura Pereira, Dorothy Bedford and Grace Stewart for expert technical assistance, to University of Porto and FCT (Portugal) for financial support (PRAXIS XXI/BD/16061/98).

References

[1] Lenfant C, Gifford RW, Zuspan FP. Consensus report: national high blood pressure education program working group report on high blood pressure in pregnancy. Am J Obstet Gynecol 1990;163:1689–712.
[2] Zeek PM, Assali NS. Vascular changes in the decidua associated with eclamptogenic toxemia of pregnancy. Am J Clin Pathol 1950;20:1099–109.
[3] Roberts JM. Endothelial dysfunction in preeclampsia. Semin Reprod Endocrinol 1998;16:5–15.
[4] Stewart DJ, Monge JC. Hyperlipidemia and endothelial dysfunction. Curr Opin Lipidol 1993;4:319–24.
[5] Pocovi M, Ordovas JM, Grande-Covian F. Plasma lipids and apolipoproteins A and B in human pregnancy. Rev Esp Fisiol 1984;40:183–90.
[6] Piechota W, Staszewski A. Reference ranges of lipids and apolipoproteins in pregnancy. Eur J Obstet Gynecol Reprod Biol 1992;45:27–35.
[7] Myatt L, Miodovnik M. Prediction of preeclampsia. Semin Perinatol 1999;23:45–57.
[8] Sattar N, Greer IA, Louden J, et al. Lipoprotein subfraction changes in normal pregnancy: threshold effect of plasma triglyceride on appearance of small, dense low density lipoprotein. J Clin Endocrinol Metab 1997;82:2483–91.
[9] Sattar N, Bendomir A, Berry C, Shepherd J, Greer IA, Packard CJ. Lipoprotein subfraction concentrations in preeclampsia: pathogenic parallels to atherosclerosis. Obstet Gynecol 1997;89:403–8.
[10] Hubel CA, Lyall F, Weissfeld L, Gandley RE, Roberts JM. Small low-density lipoproteins and vascular cell adhesion molecule-1 are increased in association with hyperlipidemia in Preeclampsia. Metabolism 1998;47:1281–8.
[11] Witztum JL. Susceptibility of low-density lipoprotein to oxidative modification. Am J Med 1993;94:347–9.
[12] Lusis AJ. Atherosclerosis. Nature 2000;407:233–41.
[13] Gordon DJ, Rifkind BM. High-density lipoprotein—the clinical implications of recent studies. New Engl J Med 1989;321:1311–6.
[14] Cockerill GW, Huehns TY, Weerasinghe A, et al. Elevation of plasma high-density lipoprotein concentration reduces interleukin-1-induced expression of E-selectin in an in vivo model of acute inflammation. Circulation 2001;103:108–12.
[15] Friedlander Y, Kidron M, Caslake M, Lamb T, McConnell M, Bar-On H. Low density lipoprotein particle size and risk factors of insulin resistance syndrome. Atherosclerosis 2000;148:141–9.
[16] Franz H, Wendler D. A controlled study of maternal serum concentrations of lipoproteins in pregnancy-induced hypertension. Arch Gynecol Obstet 1992;252:81–6.
[17] Chin JH, Azhar S, Hoffman BB. Inactivation of endothelial derived relaxing factor by oxidised lipoproteins. J Clin Invest 1992;89:10–8.
[18] Rudel LL, Kesäniemi YA. Low-density lipoprotein particle composition: what is the contribution to atherogenicity. Curr Opin Lipidol 2000;11:227–8.
[19] Campos H, Genest JJ, Blijlevens E, et al. Low density lipoprotein particle size and coronary artery disease. Arterioscler Thromb 1992;12:187–95.

[20] Kokia E, Barkai G, Reichman B, Segal P, Goldman B, Mashiach S. Maternal serum lipid profile in pregnancies complicated by hypertensive disorders. J Perinat Med 1990;18: 473–8.
[21] Rosing U, Samsioe G, Ölund A, Johansson B, Kallner A. Serum levels of apolipoprotein A-I, A-II and HDL-cholesterol in second half of normal pregnancy and in pregnancy complicated by pre-eclampsia. Horm Metab Res 1989;21:376–82.
[22] Hubel CA, McLaughlin MK, Evans RW, Hauth BA, Sims CJ, Roberts JM. Fasting serum triglycerides, free fatty acids, and malondialdehyde are increased in preeclampsia, are positively correlated, and decrease within 48 h post partum. Am J Obstet Gynecol 1996;174:975–82.
[23] Wakatsuki A, Ikenoue N, Okatani Y, Shinohara K, Fukaya T. Lipoprotein particles in preeclampsia: susceptibility to oxidative modification. Obstet Gynecol 2000;96:55–9.
[24] Parthasarathy S, Barnett J, Fong LG. High-density lipoprotein inhibits the oxidative modification of low-density lipoprotein. Biochim Biophys Acta 1990;1044:275–83.
[25] Khoo JC, Miller E, McLoughlin P, Steinberg D. Prevention of low density lipoprotein aggregation by high density lipoprotein or apolipoprotein A–I. J Lipid Res 1990;31:645–52.