Is the atherosclerotic phenotype of preeclamptic placentas due to altered lipoprotein concentrations and placental lipoprotein receptors? Role of a small-for-gestational-age phenotype

Marta R. Hentschke,*† Carlos E. Poli-de-Figueiredo,† Barbira E. Pinheiro da Costa,‡ Lesia O. Kurlak,§ Paula J. Williams,** and Hiten D. Mistry†§

Division of Women’s Health,* Women’s Health Academic Centre, King’s College London, London, UK; Laboratory of Nephrology-IPB,† School of Medicine, PUCRS, Porto Alegre, Brazil; and Department of Obstetrics and Gynaecology, School of Clinical Sciences‡ and School of Veterinary Medicine and Science,** University of Nottingham, Nottingham, UK

Abstract Atherosclerosis of spiral arteries in uteroplacental beds from preeclamptic women resemble those of atherosclerosis, characterized by increased plasma lipids and lipoproteins. We hypothesized that: 1) lipoprotein receptors/transporters in the placenta would be upregulated in preeclampsia, associated with increased maternal and fetal lipoprotein concentrations; and 2) expression of these would be reduced in preeclamptic placentae from women delivering small-for-gestational-age (SGA) infants. Placental biopsies and maternal and umbilical serum samples were taken from 27 normotensive and 24 preeclamptic women. Maternal/umbilical cord serum LDL, HDL, total cholesterol, and triglycerides were measured. Placental mRNA expression of lipidprotein receptors/transporters were quantified using quantitative RT-PCR. Protein localization/expression of LDL receptor-related protein 1 (LRP-1) in the preeclamptic placenta with/without SGA was measured by immunohistochemistry. Placental mRNA expression of all genes except PON-1, microsomal triglyceride transfer protein (MTTP), and protein disulfide isomerase family A member 2 (PDIA2) were observed. No differences for any lipoprotein receptors/transporters were found between groups; however, in the preeclamptic group placental LRP-1 expression was lower in SGA delivering mothers (n = 7; P = 0.036). LRP-1 protein was localized around fetal vessels and Hofbauer cells. This is the first detailed study of maternal/fetal lipoprotein concentrations and placental lipoprotein receptor mRNA expression in normotensive and preeclamptic pregnancies. These findings do not support a role of altered lipid metabolism in preeclampsia, but may be involved in fetal growth.—Hentschke, M. R., C. E. Poli-de-Figueiredo, B. E. Pinheiro da Costa, L. O. Kurlak, P. J. Williams, and H. D. Mistry. Is the atherosclerotic phenotype of preeclamptic placentas due to altered lipoprotein concentrations and placental lipoprotein receptors? Role of a small-for-gestational-age phenotype. J. Lipid Res. 2013. 54: 2658–2664.

Supplementary key words hypertension • lipids • low density lipoprotein cholesterol • high density lipoprotein cholesterol • triglycerides • ATP binding cassette transporter A1 • LDL receptor-related protein 1 • LDL receptor • scavenger receptor class B type 1 • fetal growth

Gestational hyperlipidemia is a common factor in pregnancy in which the maternal circulating lipid profile changes from an anabolic to a catabolic state, increasing lipids, especially triglycerides (TGs) and lipoproteins (1). From the 12th week of gestation, phospholipids, total cholesterol (TC), LDL, HDL, and TGs increase in response to estrogen stimulation and insulin resistance (2). Thus, during the first two trimesters, it is common to see maternal fat accumulation; however, in the third trimester there is enhanced lipolytic activity and decreased lipoprotein lipase (LPL) activity in the adipose tissue, consequently, fat storage declines or ceases (3). Early in gestation, the lipids are required to develop the fetal brain and central nervous system (4), to build cell membranes, and as a precursor of bile acids and steroid hormones (2). However, a maternal source of lipids is still required until term, but in lower amounts, possibly due to some fetal-derived lipids.

Abbreviations: AGA, adequate-for-gestational-age; BMI, body mass index; FGR, fetal growth restriction; FGR-M, fetal growth restriction without hemodynamic changes; FGR-S, fetal growth restriction with hemodynamic changes; IQR, interquartile range; LDL-R, LDL receptor; LRP-1, LDL receptor-related protein 1; MMP, matrix metalloproteinase; MTTP, microsomal triglyceride transfer protein; PDIA2, protein disulfide isomerase family A member 2; PON-1, paraoxonase-1; SGA, small-for-gestational-age; SRB-1, scavenger receptor class B type 1; TC, total cholesterol; TG, triglyceride.

To whom correspondence should be addressed.
e-mail: hiten.mistry@kcl.ac.uk

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from the lipogenic activity in the fetal liver, adrenal, and testes (2). Conversely, increased TGs during pregnancy have been shown to augment the risk of preeclampsia, preterm birth, and fetal growth restriction (FGR) (2, 5). The lipid metabolism and plasma levels are also affected by maternal factors such as body mass index (BMI), maternal weight gain, maternal nutrition, prepregnancy lipid levels, and various medical complications of pregnancy such as diabetes (6).

Complicating 2–8% of pregnancies, preeclampsia, along with the other hypertensive disorders of pregnancy, is one of the three leading causes of maternal morbidity and mortality worldwide (7). This disorder increases perinatal outcomes such as prematurity and FGR (8). Preeclampsia is generally defined as high blood pressure (systolic blood pressure of ≥140 mm Hg and/or diastolic blood pressure of ≥90 mm Hg) and proteinuria (≥300 mg/24 h) at or after 20 weeks gestation (9). The cause of preeclampsia remains unknown, but endothelial dysfunction, leading to compromised uteroplacental perfusion and reduced maternal-fetal transport of oxygen and nutrients is thought to be involved (10–13). Different lines of evidence indicate that abnormal lipid metabolism is involved in the pathogenesis of the disease, with acute atherosclerosis seen in preeclamptic uteroplacental beds resembling atherosclerotic lesions of coronary arteries (14). The presence of lipoprotein receptors in placental syncytiotrophoblast, specifically LDL receptor (LDL-R), LDL receptor-related protein 1 (LRP-1), and scavenger receptor class B type 1 (SRB-1) in third trimester placentae, have previously been shown (15). Placental expression of some of these receptors from FGR pregnancies with (FGR-S) and without (FGR-M) fetal hemodynamic changes, based on results of the Doppler velocimetry of umbilical artery and pulsatility index and hemodynamic changes, based on results of the Doppler velocimetry of umbilical artery and pulsatility index and from non-FGR control pregnancies have been reported. LDL-R mRNA levels in FGR-M were similar to controls but lower in FGR-S. In contrast, LDL-R protein was higher in both FGR cases than in the control group. LRP-1 mRNA and protein levels were not altered in all FGR cases. SRB-1 mRNA was unchanged in FGR, but protein levels were lower in FGR-S than in the other groups. The authors concluded that LDL-R and SRB-1 levels are altered in FGR pregnancies and maternal plasma concentrations of LDL cholesterol are higher in the control group than in the FGR-S group (15). However, these have not previously been examined in relation to preeclampsia.

Based on the literature relating to placental and liver cholesterol transport pathways, we chose to analyze the maternal and fetal lipoprotein concentrations in combination with placental mRNA expression of LRP-1, LDL-R, SRB-1, ATP-binding cassette transporter A1 (ABCA1), paraoxonase-1 (PON-1), microsomal triglyceride transfer protein (MITTP), and protein disulfide isomerase family A, member 2 (PDIA2). We therefore hypothesized that the expression of those lipoprotein receptors involved in the cholesterol pathway in the liver, are upregulated in preeclamptic placenta compared with controls as a compensatory factor. In addition, the expression of some of these receptors may be reduced in preeclamptic placentae from women delivering small-for-gestational-age (SGA) infants versus appropriate-for-gestational-age (AGA) infants.

**METHODS**

**Subjects and selection criteria**

The study population consisted of two groups of white European women (27 normotensive, 24 with preeclampsia) (Table 1). Detailed demographics and outcome data have previously been published (16). The study was approved by the Hospital Ethics Committee of the Nottingham University Hospitals; written informed consent was obtained from each participant. Preeclampsia was stringently defined as stated in the International Society for the Study of Hypertension in Pregnancy guidelines (9). Medical and obstetric histories were obtained for each participant. The corrected birthweight percentile for each infant was computed, correcting for gestational age, gender, maternal parity, and BMI (17). SGA was defined as a centile below the 10th, and AGA as an individualized birthweight ratio between the 10th and 90th percentile (18). Table 2 provides demographic, obstetric, and pregnancy description data for the preeclamptic women delivering SGA and AGA infants.

**Sample collection and measurements**

Before delivery, venous blood samples were taken from mothers and immediately after placental delivery, where possible, umbilical cord venous blood was collected. Venous samples were allowed to clot prior to centrifugation at 1,400 g for 10 min at 4°C. Serum samples were stored at −80°C prior to analysis. The number of fetal serum samples missing was 1 in the control (n = 26) and 10 in the preeclamptic (n = 14) group. All women who took part in this study were laboring and either delivered vaginally or by emergency Caesarean section.

The lipoproteins (LDL, HDL, TC, and TG) were measured using MicroSlide technology on the Vitros Fusion 5.1 Chemistry System (New York, NY) following the manufacturer’s instructions. Briefly, 200 µl of each sample were uniformly distributed over the entire slide area that contained all the reagents for the selected assays to allow larger molecules to be broken up and penetrate into the reagent layer. All samples were analyzed in triplicate, with the inter-assay variation being less than 5% and the intra-assay variation less than 10%.

Full depth placental tissue samples were collected within 10 min of the placental delivery from halfway between the cord insertion and the periphery of the placentae, avoiding infarcts. The samples were immediately rinsed in ice-cold phosphate buffered saline, and the membranes were removed and snap-frozen in liquid nitrogen for mRNA analysis. A second sample was fixed in formalin for immunohistochemistry analysis. All samples were then stored at −80°C until analysis.

**RNA extraction and cDNA synthesis**

Total RNA was extracted from a known amount of placental tissue (∼100 mg) using QiAzolysis reagent (Qiagen, Crawley, UK). RNA concentration and the quality of each gene were verified spectrophotometrically using the Nanodrop ND-1000 (Nanodrop Technologies, Labtech, Ringmer, UK); all of the samples had an A260/A280 ratio >1.96 and were stored at −80°C. RNA (1 µg) was then reverse transcribed using the QuantiTect Reverse Transcription kit containing a mix of random primers and oligo-dT (Qiagen) in a Promius 96 advanced gradient thermocycler (Peqlab Ltd., Fareham, UK).
**Quantitative real-time PCR**

Real-time PCR was carried out with the use of SYBR Green chemistry (2× QuantiFast SYBR Green, Qiagen) on a RotorGene 6000 (Corbett Research, Sydney, Australia) using the primers detailed in Table 3, following our previous protocol (19). Briefly, a pre-PCR cycle was run for 5 min at 95°C followed by 45 cycles of 95°C for 10 s, 60°C for 30 s, and 72°C for 20 s. Melt-curve analysis was performed to confirm the presence of one single product and non-template controls run to assess contamination. Cycle threshold values were used for analysis, and abundance data were obtained by the use of quantified cDNA to generate a standard curve. Standards were quantified using densitometry and 10-fold serial dilutions (10⁸ to 10¹ copies) run in parallel with the samples. Abundance data for the genes of interest were normalized to GAPDH, a stably expressed housekeeping gene suitable for normalization.

**Immunohistochemical staining of LRP-1**

LRP-1 protein expression for the 17 AGA and 7 SGA preeclampsia placentae from this cohort was analyzed by immunohistochemistry. Serial sections of placental tissue were cut (5 μm) in the same orientation from paraffin-embedded tissue blocks (Sledge Microtome, Anglia Scientific, Norwich, UK) and mounted onto SuperFrost Plus glass microscope slides (Menzel-Glaser, Braunschweig, Germany). Before use, sections were dewaxed by immersion in xylene followed by rehydration in descending concentrations of alcohol and xylene before mounting in DPX (BDH, Poole, UK).

Immunohistochemical staining was performed using the Dako Envision staining kits (Dako Ltd., Germany). LRP-1 rabbit polyclonal antibody (ARP58562_P050; Aviva Systems Biology, USA) was used for immunostaining of paraffin-embedded placental sections; the optimal dilution (1 in 500) was optimized. Heat-induced epitope retrieval was achieved by heating in a citrate buffer (pH 6.0) using a microwave oven for 15 min, followed by incubation for 30 min in normal rabbit serum (Sigma-Aldrich, UK) to block nonspecific binding; slides were then incubated with anti-LRP-1 overnight at 4°C. A negative control was performed for each test section by incubation with rabbit IgG. Sections were dehydrated and cleared in ascending concentrations of alcohol and xylene before mounting in DPX (BDH, Poole, UK).

All of the slides were assessed by the same observer, blinded to pregnancy outcome. For analysis of placental sections, digital images of five randomly selected, high-power (×400 magnification) fields were captured on NIS-Elements F2.20 microscope (Nikon United Kingdom Ltd., Surrey, UK). Quantification of LRP-1 was performed as described previously (19, 21) using the Positive Pixel Algorithm of Aperio ImageScope software. This software is able to discriminate between positive- and negative-stained pixels and combines the number of positive pixels stained with the intensity of these same pixels to produce the value “positivity.” A visual check was also performed to ensure accurate discrimination of immunolabeled regions.

**Statistical analysis**

All tests were performed using SPSS for Windows version 19. Summary data are presented as means ± standard deviation (SD) or median and interquartile range as appropriate, the Student’s t-test or Mann-Whitney U test were used depending on the distribution of the data, after testing using the Kolmogorov-Smirnov test or median and interquartile range as appropriate. Correlations between the parameters were tested with Spearman’s rank test. The null hypothesis was rejected where P < 0.05.

**RESULTS**

**Subjects**

Demographic, obstetric, and pregnancy description data of the 51 participants are shown in Table 1; clinical descriptions have previously been published (16). All patients carried singleton pregnancies and the women with preeclampsia all had moderate-to-severe disease, without HELLP syndrome. The neonates from both pregnancy groups survived. The number of fetal serum samples that were missing was 1 in the control and 10 in the preeclamptic groups.

**TABLE 2. Clinical and biochemical data of the preeclamptic women delivering AGA and SGA infants**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PE AGA (n = 17)</th>
<th>PE SGA (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age, years (mean ± SD)</td>
<td>32 ± 7.8</td>
<td>32 ± 2.9</td>
</tr>
<tr>
<td>Booking BMI, kg/m² (mean ± SD)</td>
<td>27.2 ± 4.3</td>
<td>27.1 ± 6.8</td>
</tr>
<tr>
<td>Gestational age at delivery, weeks (mean ± SD)</td>
<td>38 ± 2.5</td>
<td>35 ± 5</td>
</tr>
<tr>
<td>Birth weight, kg (median [IQR])</td>
<td>3.2 [3, 3.5]</td>
<td>2 [1.6, 2.4]   **</td>
</tr>
<tr>
<td>Birth weight centile (median [IQR])</td>
<td>47.1 [12.6, 69.4]</td>
<td>0.7 [0.3, 1.9]***</td>
</tr>
</tbody>
</table>

PE, preeclampsia; IQR, interquartile range. **P = 0.001 and ***P < 0.0001 between PE AGA and PE AGA groups.

**TABLE 3. Clinical and biochemical data of subject groups**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NC (n = 27)</th>
<th>PE (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age, years (mean ± SD)</td>
<td>30 ± 6.9</td>
<td>31 ± 6.1</td>
</tr>
<tr>
<td>Booking BMI, kg/m² (mean ± SD)</td>
<td>26.2 ± 5.4</td>
<td>26.6 ± 5.0</td>
</tr>
<tr>
<td>Maximum systolic blood pressure outside labor, mm Hg (mean ± SD)</td>
<td>116 ± 4.6</td>
<td>156 ± 7.1*</td>
</tr>
<tr>
<td>Maximum diastolic blood pressure outside labor, mm Hg (mean ± SD)</td>
<td>76.0 ± 3.0</td>
<td>98.0 ± 4.5*</td>
</tr>
<tr>
<td>Proteinuria, g/l (median [IQR])</td>
<td>6000</td>
<td>1.0 [0.3, 11.5]</td>
</tr>
<tr>
<td>Gestational age at delivery, weeks (mean ± SD)</td>
<td>40 ± 1.1</td>
<td>35.7 ± 3.8*</td>
</tr>
<tr>
<td>Birth weight, kg (median [IQR])</td>
<td>3.5 [3.3, 3.7]</td>
<td>2.9 [2.0, 3.4]*</td>
</tr>
<tr>
<td>Birthweight centile (median [IQR])</td>
<td>45 [23, 62]</td>
<td>13 [1, 82]</td>
</tr>
<tr>
<td>SGA infants [n (%)]</td>
<td>1 (3.7)</td>
<td>7 (29.2)</td>
</tr>
<tr>
<td>Precum pregnancies, ≤37 weeks gestation [n (%)]</td>
<td>0</td>
<td>14 (58.3)</td>
</tr>
</tbody>
</table>

NC, normotensive controls; PE, preeclampsia; IQR, interquartile range. *P < 0.05 between normotensive controls and women with preeclampsia.
groups. Within the preeclamptic group, 7 women delivered SGA infants and 17 delivered AGA infants (Table 2); only 1 woman in the normotensive control group delivered an SGA infant, and thus was excluded in this analysis.

Biochemical measurements

For all maternal and umbilical serum lipoproteins, there were no significant differences \((P > 0.05)\) between normotensive and preeclamptic samples. However, umbilical venous samples had significantly lower lipid and lipoprotein concentrations compared with maternal concentrations in both groups; TG (normal and preeclampsia: \(P < 0.0001\)), TC (normal and preeclampsia: \(P = 0.003\), preeclampsia: \(P = 0.01\)), and HDL (normal and preeclampsia: \(P = 0.001\)) (Fig. 1).

Placental lipoprotein receptors, transporters, and enzyme expression

The mRNA expression of \(\text{LDL-R, LRP-1, SRB-1, ABCA1, PON-1, MTTP, and PDIA2}\) in placental tissue from normotensive control and women with preeclampsia are shown in Table 4. \(\text{LDL-R, LRP-1, SRB-1, and ABCA1}\) were all found to be expressed in placenta tissue, but there was no expression of \(\text{PON-1, MTTP, and PDIA2}\). The placental mRNA expression of the receptors did not significantly differ between groups \((P > 0.05\) for all).

Although the numbers were small, we additionally analyzed the 10 late-onset preeclampsia women (>34 weeks gestation) separately against the control group to test for any gestational-specific differences. The same nonsignificant results were seen for all the maternal and fetal

<table>
<thead>
<tr>
<th>Gene</th>
<th>BLAST Sequence Accession Number</th>
<th>Primer 1</th>
<th>Primer 2</th>
<th>Length (bp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-R</td>
<td>NM_000527.3</td>
<td>5′-aggacggtacagctacc-3′</td>
<td>5′-ctccagcagcttgtagc-3′</td>
<td>73</td>
</tr>
<tr>
<td>LRP-1</td>
<td>NM_002332.2</td>
<td>5′-ggtgtaacccaccaacctat-3′</td>
<td>5′-agttgctccagcagtttcc-3′</td>
<td>88</td>
</tr>
<tr>
<td>SRB-1</td>
<td>NM_005505.4</td>
<td>5′-cataaagcagagctcttt-5′</td>
<td>5′-ctccaggcagatgttcacg-5′</td>
<td>95</td>
</tr>
<tr>
<td>PON-1</td>
<td>NM_000446.5</td>
<td>5′-atagccagagtgctcagct-5′</td>
<td>5′-ggtgtagttcagttgagg-5′</td>
<td>110</td>
</tr>
<tr>
<td>ABCA1</td>
<td>NM_005502.2</td>
<td>5′-gtctagtctcttttggact-5′</td>
<td>5′-ggtgcctctctctctcag-5′</td>
<td>76</td>
</tr>
<tr>
<td>MTTP</td>
<td>NM_000253.2</td>
<td>5′-gctctctctctctctctcag-5′</td>
<td>5′-ggtgcctctctctctctcag-5′</td>
<td>88</td>
</tr>
<tr>
<td>PDIA2</td>
<td>NM_006849.2</td>
<td>5′-gctctctctctctctctcag-5′</td>
<td>5′-ggtgcctctctctctctcag-5′</td>
<td>104</td>
</tr>
</tbody>
</table>

Fig. 1. Serum lipoprotein concentrations in maternal and fetal circulation, from normotensive controls and preeclampsia. The number of fetal serum samples that were missing were 1 in the control \((n = 26)\) and 10 in the preeclamptic \((n = 14)\). NC, normotensive control; PE, preeclampsia. Data presented as median [interquartile range]. \(*P<0.05\) between maternal and umbilical samples for all lipoproteins.
weights or gestational age at delivery were seen \( (P > 0.05) \) for both).

**Discussion**

In the present study, we have analyzed the lipid profiles in women with preeclampsia and normotensive pregnant women. To the best of our knowledge, this is the first study that has concurrently investigated the placental, maternal, and fetal lipoprotein system comprehensively in normotensive and preeclamptic pregnancies, and associated these results with SGA infants in the third trimester of pregnancy.

Previous studies have reported that hyperlipidemia is enhanced in preeclampsia (22, 23) and has a negative impact on fetal lipid profiles (24, 25). It has been suggested that dyslipidemia may contribute to the increased oxidative stress and endothelial dysfunction, and possibly insulin resistance, which causes a compensatory increase in insulin concentration, decreased LPL activity, and increased TGs. However, factors that influence preeclampsia, such as chronic hypertension, obesity, and insulin resistance, share common features with dyslipidemia related to oxidative stress and altered vascular function. Our data showed no significant differences in maternal and fetal lipoprotein concentrations between preeclampsia and normotensive controls, which is in line with previous data on maternal levels (26). In addition, in the current study the mean BMI was 26 kg/m\(^2\) in both groups (Table 1), suggesting that the abnormal lipid profile could be associated with obesity (27), and not necessarily with preeclampsia. This could also be a reason why some previous studies have reported increased lipoprotein concentrations in preeclampsia, because they may not have controlled for this. Thus, the results from this study do not suggest that changes in the lipoprotein concentrations play a direct key role in preeclampsia pathology.

All samples were collected at delivery and in the third trimester of pregnancy. Although not matched for gestation, lipoprotein concentrations were correlated with placental mRNA expression of the lipoprotein receptors, no difference between groups was found \( (P > 0.05) \). In addition, no associations between serum lipoproteins or receptors with birth weights or gestational age at delivery were seen \( (P > 0.05) \) for both.

**Table 4. Placental lipoprotein mRNA expression from normotensive controls and preeclampsia**

<table>
<thead>
<tr>
<th>Placenta Normalized mRNA Expression</th>
<th>NC (n = 27)</th>
<th>PE (n = 24)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-R (median [IQR])</td>
<td>0.05 [0.03, 0.07]</td>
<td>0.06 [0.045, 0.11]</td>
<td>0.107</td>
</tr>
<tr>
<td>LRP-1 (median [IQR])</td>
<td>7.0 [5.04, 17.33]</td>
<td>12.5 [5.23, 25.89]</td>
<td>0.503</td>
</tr>
<tr>
<td>SRB-1 (median [IQR])</td>
<td>0.34 [0.21, 0.51]</td>
<td>0.32 [0.24, 0.56]</td>
<td>0.605</td>
</tr>
<tr>
<td>ABCA1 (median [IQR])</td>
<td>31.38 [20.8, 73.55]</td>
<td>28.8 [19.32, 82.81]</td>
<td>0.942</td>
</tr>
</tbody>
</table>

NC, normotensive control; PE, preeclampsia; IQR, interquartile range.

**Fig. 2.** LRP-1 immunostaining in preeclamptic (PE) placentae from AGA delivering mothers \( (n = 17) \) (A), SGA delivering mothers \( (n = 7) \) (B), and IgG negative control (C). In photomicrographs, positive cells appear in brown; magnification ×400; scale bar = 100 μm. Protein expression was localized to Hofbauer cells (red arrows) and fetal vessels (blue arrows). In the graph, data is represented as median [interquartile range].

**Maternal serum, umbilical cord serum, and placental tissue**

When maternal and umbilical cord serum lipoprotein concentrations were correlated with placental mRNA expression of the lipoprotein receptors, no difference between groups was found \( (P > 0.05) \). In addition, no associations between serum lipoproteins or receptors with birth weights or gestational age at delivery were seen \( (P > 0.05) \) for both.

**DISCUSSION**

In the present study, we have analyzed the lipid profiles in women with preeclampsia and normotensive pregnant women. To the best of our knowledge, this is the first study that has concurrently investigated the placental, maternal, and fetal lipoprotein system comprehensively in normotensive and preeclamptic pregnancies, and associated these results with SGA infants in the third trimester of pregnancy.

Previous studies have reported that hyperlipidemia is enhanced in preeclampsia (22, 23) and has a negative impact on fetal lipid profiles (24, 25). It has been suggested that dyslipidemia may contribute to the increased oxidative stress and endothelial dysfunction, and possibly insulin resistance, which causes a compensatory increase in insulin concentration, decreased LPL activity, and increased TGs. However, factors that influence preeclampsia, such as chronic hypertension, obesity, and insulin resistance, share common features with dyslipidemia related to oxidative stress and altered vascular function. Our data showed no significant differences in maternal and fetal lipoprotein concentrations between preeclampsia and normotensive controls, which is in line with previous data on maternal levels (26). In addition, in the current study the mean BMI was 26 kg/m\(^2\) in both groups (Table 1), suggesting that the abnormal lipid profile could be associated with obesity (27), and not necessarily with preeclampsia. This could also be a reason why some previous studies have reported increased lipoprotein concentrations in preeclampsia, because they may not have controlled for this. Thus, the results from this study do not suggest that changes in the lipoprotein concentrations play a direct key role in preeclampsia pathology.

All samples were collected at delivery and in the third trimester of pregnancy. Although not matched for gestation, lipoprotein concentrations were increased between the first two trimesters and last trimester, but are then stable (28); therefore these could be compared between groups even if the gestational age was not exactly the same. Furthermore, the same nonsignificant results were seen when only the term preeclamptic samples were compared with controls.

The highest mRNA expression was \( ABCA1 \), followed by \( LRP-1 \). A previous study also reported that \( ABCA1 \) is highly expressed in human placenta (29). \( LRP-1 \) is the direct lipoprotein receptor of intermediate density lipoprotein, a
polarized cells (33). Three different mechanisms for cho-
phoblast cells efflux cholesterol from cells like any other
by the receptors; experimental evidence suggests that tro-
the placentae (Hofbauer cells).
ning that the expression is localized to the macrophages of
expressed in macrophages, and therefore it is unsurpris-
ificance, possibly due to small numbers. LRP-1 is highly
expression in the SGA group, although this didn’t reach
analyzed seven lipoprotein receptors, transporters, and
related to the cholesterol pathway, with the lipids and
SGA.

The findings of this study do not support a direct con-
tribution of lipid metabolism in the pathogenesis of pree-
lampsia. However, this is the first study that simultane-
ously analyzed seven lipoprotein receptors, transporters, and
enzymes related to the cholesterol pathway, with the lipids
and lipoprotein levels (LDL, HDL, TC, and TG) in mater-
normal and umbilical cord serum, and in relation to fetal
growth.


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