

## Dyslipidemia is a persistent problem in puerperium with or without preeclampsia

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### Summary

**Purpose of investigation:** To compare serum levels of triglycerides and cholesterol and the dyslipidemic factor (DLF): (triglycerides (mg/dl)/150) X (cholesterol (mg/dl)/200) among puerperal women with or without preeclampsia. **Materials and Methods:** Three groups of puerperal women were formed: group A uncomplicated deliveries, group B deliveries complicated with preeclampsia that had not attended the Obstetric Intensive Care Unit (OICU); and group C puerperal women complicated with preeclampsia and that had attended the OICU. **Results:** The authors studied a total of 47 puerperal women, 14 without complications, 11 complicated with preeclampsia, and 22 complicated with preeclampsia requiring attention at the OICU. Thirteen (92.8%) puerperal women without complications and 100% of puerperal women complicated with preeclampsia had triglycerides higher than 150 mg/dl at least three days post-delivery. Furthermore, six puerperal women without complications (42.8%), one puerperal woman complicated with preeclampsia (9%), and eight puerperal women complicated with preeclampsia requiring attention at the OICU (36.3%) had levels in crescendo. **Conclusions:** Hypertriglyceridemia is a persistent problem in puerperal women who suffered preeclampsia and the DLF could be a useful tool to evaluate a mixed lipemic state. Finally, preeclampsia and dyslipidemia might be considered as risk factors to develop chronic endothelial disease (CED).

**Key words:** Dyslipidemia; Preeclampsia; Puerperium.

### Introduction

Dyslipidemia includes a number of different pathological conditions whose common element is a disorder of lipid metabolism, and their subsequent alteration of the concentrations of lipids and lipoproteins in the blood. This is a common metabolic disorder during pregnancy that persists in the postpartum period (until 40 days following childbirth) and even later.

Triglycerides constitute 90% of our body fat and their normal value is 150 mg/dl. Cholesterol acts on the composition of molecules of vitamin D, hormones, and bile acids; its normal value is 200 mg/dl. Whatever the type, a lipidic disorder increases the risk of atherosclerosis and heart disease [1].

During the first two quarters of pregnancy, there is an increased lipid storage with a lipolysis similar to non-pregnant women and in later stages, as fetal nutritional demands have significantly increased, the maternal reserves decrease. The low-density lipoprotein (LDL) reaches its maximum at about 36 weeks due to liver effects of estradiol and progesterone. The high-density lipoprotein (HDL) reaches its maximum at about 25 weeks, decreases at about 32 weeks, and holds steady during the rest of pregnancy [2].

A significant percentage of pregnant women go on to develop hypertension associated with preeclampsia, dyslipidemia, gestational diabetes, and maternal obesity. The long-term consequences of these conditions have not been

adequately investigated in controlled clinical studies [3]. Unfortunately, there are limited treatment options for the possible complications to the binomial mother-child and most studies on the subject are still at an early stage [4].

In Mexico, the prevalence of metabolic diseases is rising and our concern about the high rates of maternal and infant mortality has led the authors to study the female population in the process of puerperium with persistent dyslipidemia. In the Obstetric Intensive Care Unit (OICU) of the Materno Perinatal Hospital "Monica Pretelini" (HMPMP), State Health System of the State of Mexico (ISEM), levels of cholesterol and triglycerides were monitored in all patients.

Preeclampsia, defined as the increase in blood pressure accompanied by edema, proteinuria or both, that occurs after the 20<sup>th</sup> week of gestation, is considered a diffuse endothelial disorder, which complicates 6%-10% of pregnancies [5]. This entity is characterized by increased vascular resistance, vasoconstriction, metabolic changes in nitric oxide (NO), lipids and prostaglandins, in addition to clotting abnormalities [6].

Eclampsia is defined as the development of seizures due to hypertensive encephalopathy in a preeclamptic patient, not attributed to other causes. Its incidence is close to one per 2,000 births. Seizures, which are the sign of eclampsia, are preceded by manifestations of preeclampsia, although 20% of seizures can occur up to six days after delivery [7].

Surprisingly, despite its high prevalence, information related to dyslipidemia in puerperium is scarce. Thus, further examination of the implications of dyslipidemia in puerperium is mandatory.

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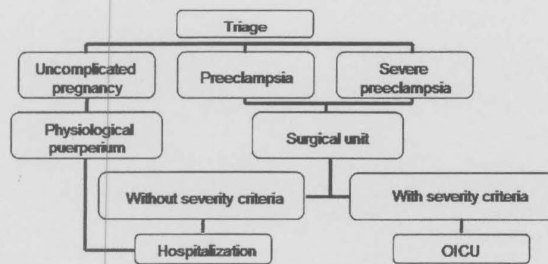


Figure 1. — Flowchart of the groups analyzed. OICU: Obstetric Intensive Care Unit.

The authors' principal aim was to compare serum levels of triglycerides and cholesterol and the dyslipidemic factor (DLF): (triglycerides (mg/dl)/150) X (cholesterol (mg/dl)/200), among puerperal women complicated or not with preeclampsia.

### Materials and Methods

This was a cohort, observational, prospective, comparative and longitudinal study developed in the HMPMP, Toluca, Mexico, during the period from August 1<sup>st</sup>, 2009 to March 30<sup>th</sup>, 2010.

#### Participants

Women in postpartum were between 16 and 46-years-old. Those with premature membrane rupture, with a previous-known chronic-metabolic disease (diabetes, pregestational dyslipidemia, and hypertension), or with incomplete medical records were excluded from this study.

Three groups were conformed: group A included puerperal women without complications (physiological puerperium), group B puerperal women complicated with preeclampsia, and group C puerperal women complicated with preeclampsia requiring attention at the OICU (Figure 1).

Preeclampsia was defined as gestational hypertension (systolic blood pressure more than 140 mm Hg and diastolic blood pressure more than 90 mm Hg) and proteinuria (at least 300 mg of urine protein in 24 h). Women requiring attention at the OICU were those with severe criteria: organ damage [8] or severe hypertension requiring i.v. drugs (sodium nitroprusside or nitroglycerin).

#### Data and measures

The data accessed in the clinical records of each patient was entered in an Excel spreadsheet previously designed by the researchers.

Blood pressure was measured with electronic monitor in the Triage room and during hospitalization.

The SPSS version 16 was used for statistical analysis. Continuous variables were expressed in means  $\pm$  standard deviation (SD). As there was no a normal distribution, the authors compared the groups using the Kruskal Wallis test and the Mann-Whitney U test for differences between two groups. A  $p \leq 0.05$  was considered statistically significant.

Table 1. — Laboratory results from the three groups analyzed.

	Group A (n = 14)	Group B (n = 11)	Group C (n = 22)
Age (years)	27.2 $\pm$ 10.1	22.9 $\pm$ 6.5	27.8 $\pm$ 7
Albumin (mg/dl)*†	3.1 $\pm$ 0.49	2.5 $\pm$ 0.6	2.9 $\pm$ 0.7
Calcium (mg/dl)	7.8 $\pm$ 0.9	7.9 $\pm$ 0.7	7.6 $\pm$ 0.6
Cholesterol (mg/dl)*	162.4 $\pm$ 4	206.6 $\pm$ 80.7	181.3 $\pm$ 54.4
Creatinine (mg/dl)†	1 $\pm$ 0.7	0.6 $\pm$ 0.1	1 $\pm$ 0.6
DLF*	1 $\pm$ 0.6	2.4 $\pm$ 2.1	1.5 $\pm$ 0.7
Glucose (mg/dl)	97.1 $\pm$ 35	105 $\pm$ 49.6	108.4 $\pm$ 49.2
Magnesium (mg/dl)	2.9 $\pm$ 0.9	2.2 $\pm$ 1	2.5 $\pm$ 0.9
Triglycerides (mg/dl)	227.9 $\pm$ 66	304.4 $\pm$ 162.7	244.4 $\pm$ 60.4
Uric acid (mg/dl)†	5.3 $\pm$ 2.4	5.1 $\pm$ 1.1	5.7 $\pm$ 1.5
VLDL (mg/dl)	46 $\pm$ 13.3	60.8 $\pm$ 32.5	48.8 $\pm$ 12
Hemoglobin (g/dl)	10.1 $\pm$ 1.5	11 $\pm$ 2.2	10.4 $\pm$ 1.8

Group A: puerperal women without complications, Group B: puerperal women complicated with preeclampsia, Group C: puerperal women complicated with preeclampsia requiring attention at the OICU; DLF: dyslipidemic factor = (triglycerides (mg/dl)/150) X (cholesterol (mg/dl)/200); OICU: Obstetric Intensive Care Unit; VLDL: very low density lipoproteins

\*:  $p \leq 0.05$  between group A and group B.

†:  $p \leq 0.05$  between group B and group C.

#### Laboratory

After delivery and for three days, with a fasting period of eight hours, the authors measured albumin (mg/dl), calcium (mg/dl), cholesterol (mg/dl), creatinine (mg/dl), glucose (mg/dl), magnesium (mg/dl), triglycerides (mg/dl), uric acid (mg/dl), and hemoglobin (g/dl). Very low-density lipoproteins (VLDL) were calculated as triglycerides (mg/dl)/5.

This study was approved by the Ethical and Research Committee of the HMPMP (date: July 2, 2009).

### Results

For the eight month period, the authors compiled complete laboratory results of 14 puerperal women without complications (median age 27.2  $\pm$  10.1 years), 11 puerperal women complicated with preeclampsia (median age 22.9  $\pm$  6.5 years), and 22 puerperal women complicated with preeclampsia requiring attention at the OICU (median age 27.8  $\pm$  7 years). Table 1 shows the laboratory characteristics of the three groups. There was a statistical significant difference in albumin and cholesterol levels between puerperal women without complications and puerperal women complicated with preeclampsia, as well as in albumin, creatinine, and uric acid between puerperal women complicated with preeclampsia and puerperal women complicated with preeclampsia who attended the OICU.

When analyzed more precisely, 13 (92.8%) puerperal women without complications, 100% of puerperal women complicated with preeclampsia, and puerperal women complicated with preeclampsia requiring attention at the OICU had triglycerides higher than 150 mg/dl at least three days post-delivery. Furthermore, six (42.8%) puerperal women without complications, one (9%) puerperal woman complicated with preeclampsia, and eight (36.3%) puerperal women complicated with preeclampsia requiring attention at the OICU had levels in crescendo.

In relation to cholesterol, two (14.2%) puerperal women without complications, six (54.5%) puerperal women complicated with preeclampsia, and 11 (50%) puerperal women complicated with preeclampsia requiring attention at the OICU had serum values higher than 200 mg/dl at least one day during post-delivery. Furthermore, five (35.7%) puerperal women without complications, two (18.1%) puerperal women complicated with preeclampsia, and nine (40.9%) puerperal women complicated with preeclampsia requiring attention at the OICU had levels in crescendo. The *p* value was of 0.027 between puerperal women without complications and puerperal women complicated with preeclampsia.

Only two (14.2%) puerperal women without complications, six (54.5%) puerperal women complicated with preeclampsia, and 11 (50%) puerperal women complicated with preeclampsia requiring attention at the OICU had both triglycerides and cholesterol levels above normal limits at least once. DLF showed a statistically significant difference between puerperal women without complications and puerperal women complicated with preeclampsia ( $p \leq 0.05$ ).

In relation to glucose, two (14.2%) puerperal women without complications, one (9%) puerperal woman complicated with preeclampsia, and two (9%) puerperal women complicated with preeclampsia requiring attention at the OICU had levels higher than 100 mg/dl. Besides the results previously commented, the anemic state of most of the women was brought to the authors' attention as Toluca City is 2,500 m above sea level and the minimum value for hemoglobin should be 12.3 g/dl [9].

## Discussion

In a normal pregnancy, serum cholesterol and triglycerides rise 25%-40% and 200%-400%, respectively. A supraphysiologic rise in plasma triglycerides' concentrations in late pregnancy may serve as a marker of prelipemia [10]. The metabolic syndrome, defined by abdominal obesity, elevation of blood pressure, fasting glucose and triglycerides, and low levels of HDL, may play an important role in the pathogenesis of unsuccessful pregnancy, by including a pro-inflammatory and prothrombotic state [11]. Inflammation in women with spontaneous preterm birth might be related to their metabolic profile, such as lipids [12]. Unfortunately, lipid profiles are not routinely measured in all pregnant women, which might indicate that the true prevalence of dyslipidemia is underestimated [13].

Several studies have examined the development of the metabolic syndrome in pregnant women [14] and there are several criteria and indexes to evaluate the repercussion of metabolic disturbances during pregnancy, such as insulin-like growth factors (IGFs), insulin-like growth factor binding proteins (IGFBPs), leptin, homeostasis model assessment (HOMA), maternal insulin sensitivity, etc. [15], but the information related to puerperium is scarce [16]. Considering the context of other work, the

authors agree that women should be followed up until 42 days postpartum [17]. Moreover, every postpartum visit should include the evaluation components of the metabolic syndrome and not only glucose intolerance [18]. In the present study the authors analyzed the post-pregnancy presence of dyslipidemia in women with physiological or complicated puerperium. The importance of this issue is emphasized by the continuous increase in the prevalence of dyslipidemia [19].

The atherogenic index of plasma (AIP =  $\text{Log}(\text{triglycerides}/\text{HDL})$ ), correlates with the size of pro- and anti-atherogenic lipoprotein particles. Clinical studies have shown that AIP predicts cardiovascular risk [20]. Although AIP is a useful cardiovascular risk marker and measure of response to treatment, it is not common to check HDL in all pregnant and puerperal women. According to the present authors' point of view, DLF proposed in this study could be a useful tool to evaluate a mixed lipemic state with a good cost-benefit approach. Certainly a study designed to obtain ROC curves for the factor suggested by the present authors to be considered in clinical practice is still missing.

Systolic hypertension and hypercholesterolemia are both considered other variables to determine the Framingham score, moreover, arterial coronary disease or equivalents or diabetes are considered as coronary risk factors. Preeclampsia, as well as the other diseases previously mentioned, produce endothelial dysfunction, in fact, preeclamptic women have an increased risk to develop this complication in a subsequent pregnancy. The authors suggest, therefore, that preeclampsia and dyslipidemia might be considered as risk factors in developing a chronic endothelial disease (CED).

Finally, several limitations to this study need to be mentioned. Firstly, this was a study with a low number of patients. Secondly, puerperal women were not systematically followed up after their delivery to take blood samples to monitor triglycerides and cholesterol levels.

## Conclusion

HDL is not usually measured in all pregnant and puerperal women. According to the authors' point of view, DLF could be a useful tool in evaluating a mixed lipemic state with a good cost-benefit approach.

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