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**Title: Correlation of biological parameters with placental parameters and pregnancy outcomes in pre-eclamptic women**

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**Abstract:**

**Introduction:** Pre-eclampsia is characterized by maternal vascular malperfusion and chronic inflammation in placenta. Our purpose was to investigate the potential correlation of biological parameters with placental parameters and pregnancy outcomes in pre-eclamptic women.

**Methods:** Pre-eclamptic women were identified by interrogation of the Medical Registry Department in six French maternities between April 2013 and June 2018. Histological parameters in placentas (weight, macroscopic and microscopic lesions), baseline maternal characteristics and pregnancy outcomes (course of pregnancy, newborns' characteristics) were collected. Biological parameters were blood cell ratios (Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Lymphocyte Ratio (NLR)) collected at delivery and Placental growth factor (PIGF) measured in women with an available first trimester serum sample. Correlations of blood cell ratios and PIGF levels with placental parameters and pregnancy outcomes were assessed by Pearson's correlation test for quantitative parameters and by logistic regression analysis for qualitative parameters.

**Results:** 202 pregnancies were included, among which 68 had a first trimester PIGF quantification. No correlation was found between biological parameters and placental lesions. Low PLR was correlated with low placental weight ( $r = 0,156$ ,  $p = 0,036$ ) and with low birth weight ( $r = 0,179$ ,  $p = 0,015$ ). Low PIGF was correlated with long time from pre-eclampsia diagnosis to delivery ( $r = - 0.250$ ,  $p = 0,048$ ).

**Conclusions:** There is no correlation between biological parameters and placental lesions in pre-eclamptic women. Yet, low PLR at delivery is correlated with low placental and birth weights. Moreover, low first trimester PIGF is correlated with long time from pre-eclampsia diagnosis to delivery.

**Key words:** pre-eclampsia, platelet to lymphocyte ratio, neutrophil to lymphocyte ratio, PlGF, birth weight, placenta.

**Abbreviations:**

Hematoxylin, Eosin and Saffron = HES

Hemolysis, elevated liver enzymes and low platelet = HELLP

Intrauterine growth restriction = IUGR

Medical Registry Department = MRD

Neutrophil-to-Lymphocyte Ratio = NLR

Placental growth factor = PlGF

Platelet-to-Lymphocyte Ratio = PLR

Soluble fms-like tyrosine kinase 1 = sFlt1

Weeks of gestation = WG

## **Manuscript:**

### **Introduction:**

Pre-eclampsia is a multifactorial pathology defined by the association of an arterial hypertension and significant proteinuria after 20 weeks of gestation (WG) [1]. It complicates around 5% of the pregnancies worldwide and is responsible for premature births and maternal morbi-mortality. During pre-eclampsia, placental implantation is abnormal. Angiogenesis impairment, resulting in a decrease in pro-angiogenic placental growth factor (PlGF) levels, has been observed at an early stage and leads to placental hypoperfusion and to chronic fetoplacental hypoxia [2-9].

An immunological conflict between mother and fetus has also been suspected in early pre-eclampsia and would result in a systemic inflammatory response in mother with pro-inflammatory cytokine production [10-13]. Maternal inflammatory biomarkers such as blood cell ratios, in particular Platelet-to-Lymphocyte ratio (PLR) and Neutrophil-to-Lymphocyte ratio (NLR), have been explored in pre-eclamptic women. At first trimester, PLR and NLR are increased in pre-eclamptic women in comparison with healthy controls [14-15], whereas at pre-eclampsia diagnosis, PLR is lowered and NLR is increased [16-18]. Low PLR has also been correlated with severity of pre-eclampsia [19,20].

Placenta is considered as a “diary of pregnancy” and reports on the course of pregnancy. Thus, pathological changes are described in placentas from pregnancies complicated with pre-eclampsia [21]. They include maternal vascular malperfusion lesions such as infarcts, placental abruption, decidual arteriopathy, hypermature villi and villous agglutination, and fetal vascular malperfusion lesions such as obliterative fetal vasculopathy and avascular villi. Chronic inflammation by mononuclear cells such as villitis of unknown etiology and chronic chorioamnionitis are also frequently seen in this context [22].

Pathological lesions are more common in case of severe preterm pre-eclampsia and seem associated with chronicity and severity of the disease [23]. Several studies have evaluated the possible association between placental parameters and biological parameters in pre-eclamptic women but none of them has explored specifically blood cell ratios. One study found a correlation between low first trimester PlGF levels and placental underperfusion lesions in women with late-onset pre-eclampsia [24]. Two other studies measuring PlGF or soluble fms-like tyrosine kinase 1 (sFlt1)/PlGF ratio at pre-eclampsia diagnosis found an association

between disrupted angiogenic biomarkers and placental lesions such as atherosclerosis, infarcts and villous changes [25,26].

In this study, we first investigated the possible correlation of blood cell ratios (i.e. PLR and NLR) at delivery and first trimester PIGF levels with placental parameters in pre-eclamptic women. In addition, we evaluated the potential correlation between those maternal blood parameters and pregnancy outcomes (i.e. course of pregnancy, newborns' characteristics).

## **Materials and Methods:**

### **Identification of pre-eclamptic women:**

The women diagnosed with pre-eclampsia were identified by interrogation of the Medical Registry Department (MRD) of Brest University Hospital and of five other maternities of our county between April 2013 and June 2018, using the following keywords: “pre-eclampsia”, “HELLP syndrome”, “eclampsia”. Pre-eclampsia was defined according to the American College of Obstetricians and Gynecologists' definition published in 2013 [1]. Severity of pre-eclampsia was assessed according to the definitions of the French experts guidelines published in 2008 [27]. Pre-eclampsia was considered as early-onset if it was diagnosed before 34 WG and as late-onset if it was diagnosed after this term.

The diagnosis of HELLP syndrome required the presence of thrombocytopenia ( $<150\,000/\text{mm}^3$ ), evidence of hepatic dysfunction (increased aspartate aminotransferase level of 40 IU/L, increased alanine aminotransferase level of 40 IU/L, or both, with increased lactate dehydrogenase (LDH) level of 600 IU/L), and evidence of hemolysis (increased LDH level, progressive anemia) [28].

Multiple gestation pregnancies were excluded from the study.

Women included in this study participated in one of two observational clinical studies on pregnancy ongoing at the same period in our county: “HPP-IPF” (NCT02884804) and “HEMOTHEPP” (NCT02443610).

### **Placental parameters:**

Histopathological examination of the placentas had been performed by two senior perinatal pathologists at Brest University Hospital. Histological findings were recorded by interrogation of the pathology computerized database APIX V7.

Placentas were fixed in 4% buffered formalin. Standard sampling of three blocks in the central area was performed and slides were Hematoxylin, Eosin and Saffron (HES) stained.

Recorded macroscopic findings corresponded to the following items: placenta weight, fetoplacental weight ratio, placental abruption, abnormal placental set-up (only circumvallation), abnormal umbilical cord (villamentous implantation, thin umbilical cord with < 0,8 cm in diameter, presence of a knot), presence and number of placental infarcts, intervillous thrombi and thrombi in a vessel of the chorionic plate affecting  $\geq$  one third of the placental surface.

Recorded microscopic lesions corresponded to the following items according to Amsterdam consensus [29]: maternal vascular malperfusion lesions such as microscopic infarcts, decidual arteriopathy, abnormal villous maturation (hypermature villi or villous agglutination), presence of fetal vascular malperfusion signs such as obliterative fetal vasculopathy or avascular villi, chorangiosis and erythroblastosis, excessive fibrin deposition, chronic inflammation such as villitis or chronic intervillitis of unknown etiology, chronic chorioamnionitis or chronic deciduitis.

### **Pregnancy outcomes:**

The following data were recorded from medical files on a computerized database: baseline maternal characteristics including preconceptional Body Mass Index, tobacco use, medical history (chronic hypertension, chronic nephropathy, diabetes, cardiovascular disease, sickle cell disease, autoimmune disease, previous venous thromboembolism, known biological thrombophilia), blood and rhesus group, obstetrical history, especially previous pre-eclampsia, age at delivery, first degree familial history of chronic hypertension and cardiovascular disease. The following pregnancy characteristics were also collected: method of conception, medication during pregnancy (in particular aspirin, heparin, hydroxychloroquine or corticosteroids), gestational diabetes, intrahepatic cholestasis of pregnancy, premature rupture of membrane, term at diagnosis of pre-eclampsia, term at delivery and method of delivery, presence of a pre-eclampsia severity criterion, postpartum complications including worsening of pre-eclampsia, postpartum hemorrhage and thromboembolic event, intensive care admission and length of stay. Time from pre-eclampsia

diagnosis to delivery was determined and considered as a prognostic marker in pre-eclamptic pregnancies.

Postpartum complications were defined as worsening of pre-eclampsia signs after delivery, postpartum hemorrhage (defined by a blood loss > 500 ml, whatever the mode of delivery) [30] or a thromboembolic event after delivery and before hospital discharge.

The following fetal characteristics were recorded: presence of intrauterine growth restriction (IUGR), stillbirth, birthweight and sex of the newborn. IUGR was defined according to the 2013 French College of Obstetricians and Gynecologists guidelines by an estimated fetal weight below the 10<sup>th</sup> percentile using locally-accepted curve (AUDIPOG) associated with signs of fetal growth pathological restriction [31].

### **Biological parameters:**

Blood cell counts were collected at delivery from medical files in order to calculate PLR and NLR at delivery for each woman.

PIGF quantification was performed from available blood samples collected at the end of first trimester of pregnancy (between 11 WG and 13+6 WG) for Down syndrome screening and stored at -20°C in Biochemistry department of Brest University Hospital. Measurements were achieved with the automated B·R·A·H·M·S KRYPTOR compact PLUS system (B·R·A·H·M·S PIGF plus KRYPTOR: Thermo Fisher Scientific, Hennigsdorf, Berlin) according to the manufacturer's instructions described elsewhere [32]. PIGF levels were expressed in pg/ml.

The institutional review board of Brest University Hospital approved "HPP-IPF" and "HEMOTHEPP" studies. Informed oral consents were obtained from all participants. We excluded women who had expressed their opposition to participate to the study. Informed written consents were obtained from women whose blood samples had been collected at the end of first trimester.

### **Statistical analysis:**

Quantitative variables were summarized using median and interquartile range. Categorical variables were summarized as frequency (%) of categories.



Correlations between first trimester PIGF levels, blood cell ratios (PLR and NLR) at delivery and quantitative variables were assessed by Pearson's correlation test and expressed with rho coefficient (r), p value and 95% confidence interval (CI). Statistical significance was set at  $p < 0,05$ .

Correlations between biological parameters and qualitative variables were assessed by a logistic regression analysis and expressed by an Area Under the Receiver Operating Characteristics (AUROC), an Odd Ratio (OR) and a 95%CI.

All quantitative parameters were evaluated in the correlation analysis, whereas only frequent qualitative parameters were included in the logistic regression analysis.

All statistical analyses were performed with XLSTAT [33].

## **Results:**

### **General characteristics:**

551 pregnancies complicated by pre-eclampsia or Hemolysis, elevated liver enzymes and low platelet (HELLP) syndrome were identified after interrogation of the MRD during the study period (*cf figure 1*).

Among these 551 pregnancies, after exclusion of multiple gestation pregnancies and of duplicates, only 202 pregnancies had both a blood cell count at delivery and an available placental histological examination. Five women were included twice for two consecutive pregnancies complicated with pre-eclampsia.

Among these 202 pregnancies, 68 had a first trimester available serum sample for PIGF quantification.

Baseline maternal characteristics of the 197 women are detailed in **table 1**. Maternal and fetal characteristics of the 202 pregnancies complicated with pre-eclampsia are detailed in **table 2**.

66,3% of the women had a severe pre-eclampsia, 49,5% had an early pre-eclampsia and 48% of pre-eclampsia cases were associated with IUGR. Median time from pre-eclampsia diagnosis to delivery was two days, with a minimum of zero day to a maximum of 29 days.

The description of histological features of the 202 corresponding placentas is presented in **Table 3**.

### **Correlation analysis:**

Qualitative pregnancy outcomes (present or absent) selected for the correlation analysis were the following: severe pre-eclampsia, gestational diabetes, placental abruption, HELLP syndrome, IUGR, postpartum complications, intensive care admission of the mother.

Other collected pregnancy outcomes were not analyzed because they were infrequent.

### **Blood cell count at delivery:**

No correlation was found between PLR or NLR at delivery and placental histological parameters in the 202 pregnancies complicated with pre-eclampsia (*cf table 5*).

Low PLR at delivery was correlated with low placenta weight ( $r = 0,156$ ;  $p = 0,036$ ;  $95\%CI = 0,011-0,295$ ) and low newborn weight ( $r = 0,179$ ,  $p = 0,015$ ,  $95\%CI = 0,035-0,317$ ).

No correlation was found between PLR or NLR at delivery and qualitative pregnancy outcomes.

### **First trimester PIGF levels:**

The average first trimester PIGF value was 33,66 pg/ml. The median PIGF value was 26,69 pg/ml (minimum = 10,49 pg/ml ; maximum = 112,40 pg/ml).

No significant correlation was found between first trimester PIGF levels and histological parameters in placentas of the 68 pre-eclamptic women who had an available first trimester serum sample (*cf table 4*).

Yet, low first trimester PIGF was correlated with long time from pre-eclampsia diagnosis to delivery ( $r = - 0.250$ ,  $p = 0,048$ ).

No correlation was found between first trimester PIGF levels and qualitative pregnancy outcomes.

### **Discussion:**

In this study, we aimed to assess a possible correlation of maternal blood parameters with placental parameters and pregnancy outcomes in the context of pre-eclampsia. Due to impaired angiogenesis, inflammatory and procoagulant state observed in pre-eclamptic women, we hypothesized that first trimester PIGF levels and blood count ratios at delivery would be correlated with placental parameters. We noted a correlation between PLR at delivery and placenta weight as well as birth weight in pre-eclamptic women. We did not find any correlation between first trimester PIGF levels and placental parameters but we observed a correlation between PIGF levels and time from pre-eclampsia diagnosis to delivery.

Blood count cell is an available and low-cost biological test. Blood cell ratios (PLR and NLR) seem to be sensitive biomarkers for systemic inflammation, as attested by their relevance in sepsis [34-36], chronic viral hepatitis [37], acute pancreatitis [38], systemic vasculitis [39] and auto-immune diseases [40,41]. No study evaluated the possible correlation of blood cell ratios with placental parameters in the context of pre-eclampsia. One Turkish study explored the link between blood cell ratios and birth weight in 783 healthy singleton pregnancies [42]. The authors found that low NLR and low PLR were correlated with a high birth weight. On the contrary, in our pre-eclamptic population, we found that low PLR was correlated with low birth weight, *i.e.* a poor pregnancy outcome, what has already been described in preterm births of any etiology [43]. The negative correlation between PLR and pre-eclampsia severity noted in some studies [19,20] is also concordant with our findings and plaid for a pejorative value of a low PLR at pre-eclampsia diagnosis or at delivery in pregnant women. Thus, it is known that a low platelet count is a severity criterion for pre-eclampsia, given that it reflects coagulation activation and systemic thrombotic microangiopathy.

Only one study in the literature evaluated the possible correlation of first trimester PIGF levels with placental histological lesions in 73 pre-eclamptic women [24]. The authors described an association between low first trimester PIGF levels and histological findings attributable to placental underperfusion, what is consistent with the early angiogenesis impairment observed in pre-eclampsia [4]. We did not confirm those findings, probably because of a difference in methodology and in statistical analysis between the two studies.

We observed a correlation between low first trimester PIGF levels and long time from pre-eclampsia diagnosis to delivery. To our knowledge, no study evaluated the correlation of first trimester PIGF levels with time from pre-eclampsia diagnosis to delivery. Kose *et al* [44] investigated sFlt1/PIGF ratio at pre-eclampsia diagnosis in 50 women and found that a high

sFlt1/PlGF ratio was associated with a long time from pre-eclampsia diagnosis to delivery, what is concordant with our findings. Time from pre-eclampsia diagnosis to delivery could be regarded as a prognostic marker in pre-eclampsia. Indeed, time from pre-eclampsia diagnosis to delivery is usually longer when pre-eclampsia is mild at diagnosis and doesn't require an urgent induced delivery because of pejorative maternal or fetal parameters.

Our study has some strengths. We explored the possible correlation between blood cell ratios at delivery and placental parameters in pre-eclamptic women, what has not been described elsewhere. Then, two senior perinatal pathologists analyzed all placentas and applied validated, standardized and reproducible histological criteria for placental lesions classification. Finally, this is a multicenter study, what partly prevents from recruitment bias.

Our study has some weaknesses. First, due to its retrospective design, it contains a bias of selection related to placenta addressing for histological analysis. Second, the sub-group of pre-eclamptic women who had first trimester PlGF quantification is small, what could partly explain why we did not find any correlation between PlGF levels and placental parameters. Finally, pre-eclamptic women at risk of preterm delivery received corticosteroids in order to accelerate fetal lung maturity. Yet, it is well known that corticosteroids have an impact on blood cell count, by lowering lymphocyte count and increasing platelet count. This could have introduced another bias in our study, especially for the blood cell ratio correlation analysis.

A prospective study with more women addressing the same question in the context of pre-eclampsia, *i.e.* the possible correlation of maternal biological parameters with placental parameters and pregnancy outcomes, would enable to avoid biases encountered in our study. Thus, in a cohort study enrolling pregnant women from first trimester of pregnancy, all women could have a systematic blood sample analysis at each trimester of pregnancy for PlGF quantification and blood cell count, and all placentas could be analyzed by a trained pathologist. Such a project would support interprofessional collaboration in women health care. Previous extensive studies evaluating first trimester PlGF dosage for pre-eclampsia prediction could also help to address our question, if a standardized placental histological examination was available for each woman.

In summary, blood cell ratios and first trimester PlGF levels are not correlated with placental lesions in pre-eclamptic women. Yet, in pre-eclampsia, low PLR at delivery is correlated with low placenta weight and low newborn weight. Moreover, low first trimester PlGF is correlated with long time from pre-eclampsia diagnosis to delivery.

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Thermofisher Scientific did not interfere with the study design, with the data analysis and interpretation or with the writing of the manuscript.

## **Tables:**

**Table 1:** Baseline characteristics of the 197 women.

<b>n = 197 women for 202 pregnancies</b>	
Median age at delivery	30 (18-46)
Cigarette smoking	52 (25.7%)
Medical history	
Chronic hypertension	14 (6.9%)
Chronic nephropathy	10 (5%)
Diabetes	4 (2%)
Cardiovascular disease	3 (1.5%)
First-degree familial history of chronic hypertension	48 (23.8%)
First-degree familial history of cardiovascular disease	14 (6.9%)
Auto-immune disease	12 (5.9%)
Systemic lupus erythematosus	1 (0.5%)
Antiphospholipid syndrome	4 (2%)
Hashimoto thyroiditis	3 (1.5%)
Crohn disease	4 (2%)
Previous venous thromboembolism	6 (3%)
Biological thrombophilia other than APS	9 (4.5%)
First-degree familial history of venous thromboembolism	15 (7.4%)
Median BMI before pregnancy	24 (16-58)
Obstetrical history	
Nulliparous	117 (57.9%)
Multiparous without pre-eclampsia	56 (27.7%)
Multiparous with pre-eclampsia	29 (14.4%)
≥ 2 miscarriages	12 (5.9%)
Blood group	
O group	87 (43.1%)
Negative rhesus	33 (16.3%)

Continuous variables are expressed as medians, with minimum and maximum values between brackets, and categorical variables are expressed as frequencies (percents). APS = antiphospholipid syndrome; BMI = body mass index.

**Table 2:** Maternal and fetal characteristics of the 202 pregnancies

<b>n = 197 women for 202 pregnancies</b>	
<b>Maternal side</b>	
Method of conception	
Natural	189 (93.6%)
Assisted	13 (6.4%)
Medication use during pregnancy	
Aspirin	22 (10.9%)
Heparin/LMWH	12 (5.9%)
Immunosuppressive agent	4 (2%)
Gestational diabetes	39 (19.3%)
Thromboembolic event during pregnancy	1 (0.5%)
Intrahepatic cholestasis of pregnancy	2 (1%)
Median term at diagnosis of pre-eclampsia (WG)	34 (22-41)
Early pre-eclampsia	100 (49.5%)
Severe pre-eclampsia	134 (66.3%)
Eclampsia	3 (1.5%)
Placental abruption	23 (11.4%)
HELLP syndrome	59 (29.2%)
DIVC	5 (2.5%)
Median term at delivery (WG)	35 (22-41)
Median time from pre-eclampsia diagnosis to delivery (WG)	2 (0-29)
Delivery by cesarean section	143 (70.8%)
Post-partum complications	54 (26.7%)
Worsening of pre-eclampsia	42 (20.8%)
Post-partum haemorrhage	17 (8.4%)
Post-partum thromboembolic event	1 (0.5%)
Intensive care admission in postpartum	33 (16.3%)
Median stay duration in ICU (day)	3 (1-9)
<b>Fetus/Newborn side</b>	
Abnormal uterine artery doppler	62 (30.7%)
Abnormal umbilical artery doppler	42 (20.8%)
Abnormal cerebral artery doppler	25 (12.4%)
Oligohydramnios	16 (7.9%)
IUGR	97 (48%)
Birth weight < 3 <sup>rd</sup> percentile	44 (21.8%)
Stillbirth	6 (3%)
Birth weight (grams)	1850 (350-4230)
Birth weight (percentiles)	15.2 (0-95.1)
Sex	
Male	99 (49%)
Female	102 (50.5%)

Continuous variables are expressed as medians, with minimum and maximum values between brackets, and categorical variables are expressed as frequencies (percents). LMWH = low molecular weight heparin; WG = weeks of gestation; DIVC = disseminated intravascular coagulation; ICU= intensive care unit; IUGR = intrauterine growth restriction.

**Table 3:** Histological characteristics of the 202 placentas

<b>Macroscopic findings</b>	<b>All placentas (n = 202)</b>
Median placenta weight (grams)	<b>350 (80-755)</b>
Median fetoplacental weight ratio	<b>5.4 (0.4-9.7)</b>
Abnormal placental set-up	<b>10 (5%)</b>
Abnormal umbilical cord	<b>43 (21.3%)</b>
Placental macroscopic infarcts	<b>127 (62.9%)</b>
If present, median number	<b>2 (1-14)</b>
Placental abruption	<b>13 (6.4%)</b>
Intervillous thrombi	<b>10 (5%)</b>
Thrombi in a vessel of the chorionic plate affecting $\geq 1/3$ of the placental surface	<b>6 (3%)</b>
<b>Microscopic findings</b>	
<b>Maternal vascular malperfusion lesions</b>	<b>179 (88.6%)</b>
Decidual arteriopathy	<b>4 (2%)</b>
Microscopic infarcts	<b>12 (5.9%)</b>
Hypermature villi	<b>147 (72.8%)</b>
Villous agglutination	<b>14 (6.9%)</b>
<b>Fetal vascular malperfusion lesions</b>	<b>79 (39.1%)</b>
Obliterative fetal vasculopathy	<b>12 (5.9%)</b>
Avascular villi	<b>44 (21.8%)</b>
Chorangiosis	<b>34 (16.8%)</b>
Erythroblastosis	<b>6 (3%)</b>
<b>Excessive fibrin deposition</b>	<b>108 (53.5%)</b>
<b>Inflammation</b>	<b>64 (31.7%)</b>
Villitis of unknown etiology	<b>15 (7.4%)</b>
Chronic intervillitis of unknown etiology	<b>4 (2%)</b>
Chronic chorioamnionitis	<b>43 (21.3%)</b>

Continuous variables are expressed as medians, with minimum and maximum values between brackets, and categorical variables are expressed as frequencies (percents).



**Table 4:** Correlation analysis of first trimester PIGF levels with quantitative placental parameters and quantitative pregnancy outcomes in the 68 pre-eclamptic women with an available first trimester serum sample.

Placental parameters	1 <sup>st</sup> T PIGF		
	r	p	95%CI
Placenta weight (grams)	0.074	0.564	-0.177, 0.316
Number of macroscopic infarcts	-0.113	0.378	-0.351, 0.139
Pregnancy outcomes	r	p	95%CI
Birth weight (grams)	0.162	0.205	-0.089, 0.394
Term at pre-eclampsia diagnosis (WG)	0.155	0.226	-0.097, 0.388
Term at delivery (WG)	0.101	0.432	-0.151, 0.340
Time from pre-eclampsia diagnosis to delivery (day)	<b>-0.250</b>	<b>0.048</b>	<b>-0.469, -0.003</b>

Results of the Pearson's correlation test are expressed with rho coefficient r, p value and 95%CI. PIGF = placental growth factor. WG = weeks of gestation, 1<sup>st</sup> T = first trimester of pregnancy.

**Table 5:** Correlation analysis of blood cell ratios (PLR and NLR) at delivery with quantitative placental parameters and quantitative pregnancy outcomes in the 202 pregnancies complicated with pre-eclampsia.

*Cf* Word file joined for table 5

**Figures:**

**Figure 1:** Flow chart of the study

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**Table 5:** Correlation analysis of blood cell ratios (PLR and NLR) at delivery with quantitative placental parameters and quantitative pregnancy outcomes in the 202 pregnancies complicated with pre-eclampsia.

Histological placental parameters	PLR			NLR		
	r	p	95%CI	r	p	95%CI
Placenta weight (grams)	<b>0.156</b>	<b>0.036</b>	<b>0.011, 0.295</b>	-0.013	0.865	-0.158, 0.133
Number of macroscopic infarcts	0.089	0.233	-0.057, 0.231	0.046	0.539	-0.100, 0.190
Pregnancy outcomes	r	p	95%CI	r	p	95%CI
Birth weight (grams)	<b>0.179</b>	<b>0.015</b>	<b>0.035, 0.317</b>	-0.039	0.603	-0.183, 0.107
Term at pre-eclampsia diagnosis (WG)	0.142	0.056	-0.004, 0.281	-0.074	0.321	-0.217, 0.072
Term at delivery (WG)	0.140	0.059	-0.005, 0.280	-0.113	0.128	-0.254, 0.033
Time from pre-eclampsia diagnosis to delivery (day)	0.014	0.854	-0.132, 0.159	-0.138	0.064	-0.278, 0.008

Results of the Pearson's correlation test are expressed with rho coefficient r, p value and 95%CI. WG = weeks of gestation.