

The Association Between Resistivity Index (IR) and the sFlt-1 and PlGF Values in Pregnant Women With Risk of Preeclampsia

GEORGE TOTH^{1#}, MARIUS CRAINA¹, LAVINIA STELEA^{1#}, COSMIN CITU¹, RADU NEAMTU¹, ATILA FOGOROSSY¹, RADU DUMITRU MOLERIU^{2*}, RAZVAN BARDAN^{3#}, IZABELLA PETRE^{1*}, RAZVAN SUSAN¹, ADELINA CHEVERESAN¹, NICOLAE SUCIU⁴

¹Victor Babes University of Medicine and Pharmacy, Department XII, Discipline of Obstetrics and Gynecology, 2 Eftimie Murgu Sq 300041, Timisoara, Romania

² West University of Timisoara, Faculty of Mathematics and Computer Science, Department of Mathematics, ROMANIA

³Victor Babes University of Medicine and Pharmacy, Department XV, Discipline of Urology, 2 Eftimie Murgu Sq 300041, Timisoara, Romania

⁴ Carol Davila University of Medicine and Pharmacy, Department of Obstetrics and Gynecology, Alfred Rusescu Institute for Mother and Child Care, Bucharest, Romania

Worldwide, 5-8% of pregnant women are diagnosed with preeclampsia. This disease increases the morbidity and mortality of the fetus and pregnant woman, especially in developing countries. Preeclampsia is characterized by systolic blood pressure > 140mmHg or diastolic blood pressure > 90mmHg as measured twice, and 24 h proteinuria ≥ 0.3 g, after 20 weeks of gestation. The cause of preeclampsia is still incompletely elucidated. Numerous studies have suggested to modernize the definition of preeclampsia by incorporating key biomarkers of either placental or vascular origins, including placental growth factor (PlGF) and antiangiogenic factors such as tyrosine kinase-1 (sFlt-1) in the diagnosis of preeclampsia and the risk of occurrence of the disease in the second trimester of pregnancy [1-5]. We studied a group of 50 patients with a 21-week pregnancy diagnosis, we calculated the ratio between sFlt-1 and PlGF and we tested to see if there was an association between this ratio and the resistivity index (IR) of the uterine artery using the artery Doppler ultrasound. The PlGF level in our group was decreased in women who developed preeclampsia compared to the control group where this problem did not occur. Doppler ultrasound examination during the second trimester of pregnancy may provide extra data for prediction of preeclampsia. Although much of pathophysiology of preeclampsia has been explained, the exact etiology of this disorder remains unclear. It is certain that before the clinical signs of preeclampsia are detectable, there is an imbalance between pro-angiogenic and anti-angiogenic factors.

Keywords: placental growth factor, tyrosine kinase-1, preeclampsia, uterine artery resistivity index

Over the last decade, the definition of preeclampsia was revisited as the mechanisms underlying the disease were dramatically evolved. [6-8]. The exact pathophysiology of preeclampsia remains undefined. There are many studies that support the hypothesis that the occurrence of this pathology would be due to an insufficient placental perfusion that would result from an abnormal remodeling of the maternal spiral arteries [9-13].

In preeclampsia, the maternal placental growth factor (PlGF) is decreased, while the serum level of tyrosine kinase-1 (sFlt-1) is increased.

A PlGF's antagonist, the soluble vascular endothelial growth factor receptor 1 (sFlt-1) causes vasoconstriction and endothelial lesions that can lead to intrauterine growth restriction and preeclampsia. High sFlt-1/PlGF ratio is associated with an increased risk of preeclampsia and can be a better predictor of preeclampsia than any other biomarker [14-16]. Angiogenic and anti-angiogenic factors have been implicated in the pathophysiology of preeclampsia. In general, the t-1/PlGF ratio appears to show better performance than single markers [17,18]. Some studies support the theory that starting low-dose aspirin before 16 weeks of gestation would benefit pregnancy, reducing the risk of preeclampsia [19,20].

Experimental part

Material and methods

For this study we gathered information from 50 patients. We have a homogenous sample: all the patients are pregnant in week 21 and they all were submitted to the same medical tests. The database was collected using an Excel file. The statistical analysis was run using the SPSS program and for the charts and tables we used the Microsoft Excel program. In the first part of our study we tested the distribution of the data. Further on, we wanted to see if there are any differences between the body mass index (BMI) before pregnancy and now (in week 21) and the BMI in patients with or without preeclampsia. We calculated a report between the sFlt-1 and PlGF values and we tested to see if there is an association between this report and the resistivity index (IR). As well, we have information about the patients age, environment, the Doppler values in week 21 and if they are smokers or non-smokers. For the statistical tests we applied the Mann-Whitney test and for the association of values we calculated the Pearson coefficient and we applied a regression model for this data. The significance level is considered $\alpha=0.05$.

*email:radu.moleriu@e-uvf.ro; Phone:0040745511314
email:dr.petreizabella@yahoo.com; Phone:0040722646058

#Authors with equal contribution.

Results and discussions

In this study, as we mentioned before, we have tested 50 patients. For a better characterization of our sample we run some descriptive statistics on the numerical data (table 1) and we plotted the main results (fig. 1, 2). From our 50 patients, 19 patients (38%) are non - smoker and 31 patients (62%) are smokers.

Further on, for the statistical analysis, as we mentioned before, we tested to see if we have normal distribution in our data. For this, we applied the Kolmogorov - Smirnov normality test and we obtained that our data are not normally distributed ($p < 0.05$). So, using the Man-Whitney test we wanted to see if the differences observed in the BMI before pregnancy and now (week 21) can be considered significant. After applying the test we obtained $p = 0.38 > 0.05$, so we can conclude that even if we have a higher BMI in week 21 this differences are not statistically significant. Another major classification is made behalf the

presence / absence of preeclampsia. For all numerical variables which we tested in this classification we obtained significant differences only in the case of BMI and in the case of the sFlt-1 values ($P < 0.05$). So, we can say that the patients who developed preeclampsia have a significantly higher BMI and a significantly higher sFlt-1 value. The last statistical test was run to see if the smoking habit alone can influence the dynamics of the tested data. After applying the Mann - Whitney test on all numerical data (age, BMI before and now, Doppler, sFlt-1, PIGF, report and IR) we obtained insignificant differences ($p > 0.05$) in all cases. So, the smoking habit alone can't be considered a trigger in this case.

In the last part of this study, we tested to see if we can find an association between the calculated report (the report was obtained by dividing the sFlt-1 values to the PIGF values) and the resistivity index (IR) and between the Doppler and the IR values, both obtained in week 21.

Table 1

WE CALCULATED THE CENTRAL TENDENCY AND DISPERSION INDICATORS FOR THE NUMERICAL DATA INCLUDED IN THE STUDY.

Statistics	Age	BMI before	Actual BMI	Doppler 21 weeks	sFlt-1	PIGF	Report	IR
Mean	31.40	25.20	26.16	0.52	1526.57	174.75	11.92	0.8452
Standard Error	0.67	0.76	0.80	0.02	84.60	17.09	1.10	0.01
Median	32	23.81	24.45	0.52	1489	134.55	10.29	0.85
Mode	29	23.53	21.09	0.43	1009	101		0.85
Standard Deviation	4.77	5.36	5.64	0.12	598.19	120.82	7.77	0.06
Sample Variance	22.73	28.69	31.85	0.01	357831.93	14597.29	60.30	0.00
Kurtosis	-0.90	2.00	1.42	-1.15	-0.01	5.77	0.23	-0.58
Skewness	-0.09	1.43	1.27	0.07	0.51	2.10	0.97	0.00
Range	19	24.76	25.18	0.44	2411.10	648.8	30.63	0.2
Minimum	22	18.37	19.43	0.34	486.90	36	2.48	0.75
Maximum	41	43.13	44.62	0.78	2898.00	684.80	33.11	0.95
Sum	1570	1259.79	1308.14	26.11	76328.30	8737.30	596.14	42.26
Count	50	50	50	50	50	50	50	50

The distribution of BMI before and during pregnancy

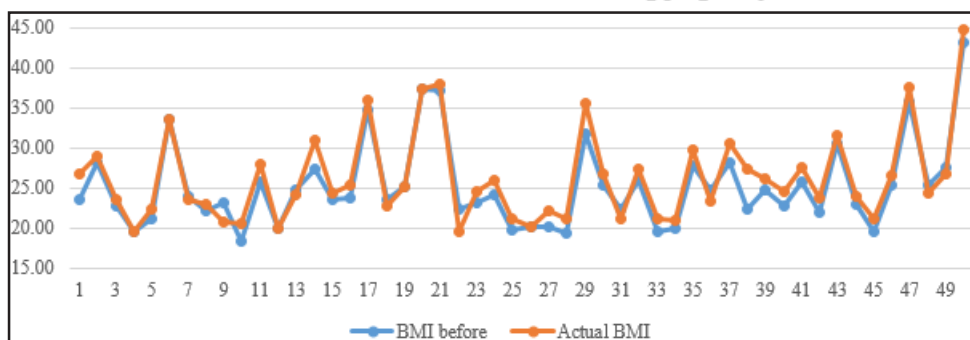


Fig. 1. The dynamics of the BMI before pregnancy and in week 21.

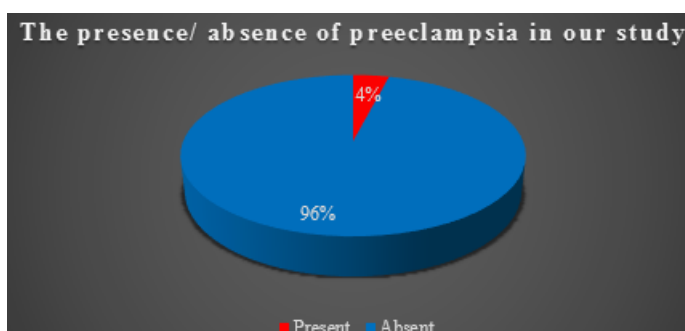


Fig.2 The presence/absence of preeclampsia, a major complication that can be seen during pregnancies.

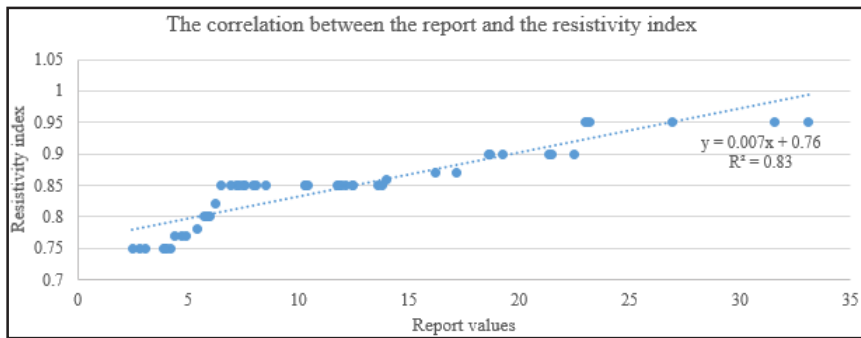


Fig. 3 The association between the report values and the resistivity index values.

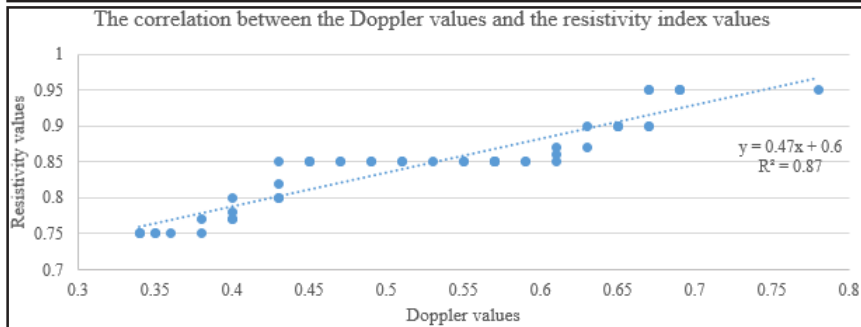


Fig. 4 The association between the Doppler values and the resistivity index values

For this, we calculated the Pearson coefficient and we applied a regression model in both scenarios. In both cases we obtained a very strong positive correlation ($r_1=0.91$, $r_2=0.93$). The determination coefficients are $R_1=0.83$ and $R_2=0.87$ and for the significance we obtained a $p<0.001$, which will conduce as to the conclusion that the observed association is extremely significant. This associations are plotted in figures 3,4.

Conclusions

After applying the statistical tests we can say that we have a very strong positive association between the sFlt-1, PlGF values and the IR values and between the Doppler and the IR values in week 21.

Pregnancy is a physiological condition for women, and the percentage of physical activity decreases. During this period, lifestyle changes in general and often tends to change over time. The progressive accumulation of chronic metabolic diseases and cardiovascular disease is usually inevitable.

More and more studies raise the theory of arterial stiffness resulting from a degenerative process that primarily affects the extracellular matrix of elastic arteries under the effect of aging. The properties of arterial elasticity are increasingly used to stratify the risk in many populations, and recently ESH / ESC recommends pulse rate (PWV) for the monitoring of high blood pressure, which is considered a *gold standard* for assessing arterial stiffness [21-27]. In our study, as well, we found a significant connection between the BMI and the appearance of preeclampsia. A high BMI value can increase the chance of developing preeclampsia during pregnancy.

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