The role of sFLT-1 and PI GF factors as well as the sFLT-1/PI GF ratio as a predictor of gestational hypertension and preeclampsia

MAREK CHUCHRACKI1, MARIOLA KRZYŚCIN2, ANNA DERA-SZYMANOWSKA2, MAGDALENA PISARSKA1, EWA FLOREK3, GRZEGORZ H. BRĘBOROWICZ2

Abstract
Objective: To evaluate the usefulness of the concentration of soluble fms-like tyrosine kinase 1 (sFlt-1), placental growth factor (PlGF), and the sFLT-1/PlGF ratio to identify patients suffering from hypertensive complications at a later stage of pregnancy in an increased risk patients. Method: In a group of 322 pregnant women, PlGF and sFlt-1 were assessed during three periods of pregnancy: 1. 11-14 gw, 2. 20 ± 2 gw 3. 30 ± 2 gw. After the delivery and analysis of medical records, the patients were assigned to three groups: control group (0) with normal blood pressure during the entire pregnancy (196; 61.4%); 1 – female patients who were diagnosed with gestational hypertension after 20 gw without significant proteinuria (107; 33.5%); 2 – patients with preeclampsia – hypertension and proteinuria > 300 mg/24 h (16; 5.0%). Results: There were no differences in the concentrations of PlGF and sFlt-1 between the studied groups in the 1st trimester of pregnancy. At 20 ± 2 gw, a significant decrease in PI GF in women with hypertensive complications was observed along with an increase in sFlt-1/PlGF ratio in women with preeclampsia when compared to women with gestational hypertension and healthy patients. The 30 ± 2 pregnancy weeks was associated with a significant increase in sFlt-1, a decrease in PI GF and an increase in the sFLT-1/PlGF ratio in pregnant women with hypertension and preeclampsia. The usefulness of sFlt-1 and PI GF concentrations was assessed for the detection of hypertensive complications in later pregnancy in each trimester. In 20 ± 2 gw, the area under the ROC curve for PI GF had a substantial value and amounted to AUC 62% for sFlt-1/PlGF AUC = 60% (p < 0.05). In 30 ± 2 gw, AUC=87% for PI GF, and AUC = 87% for sFlt-1/PlGF (p < 0.001). Conclusion: Low concentrations of PlGF and an increased value of the sFLT-1/PlGF ratio starting from the second trimester of pregnancy may be important predictor of hypertensive complications, and help in diagnosing this group of diseases before the onset of clinical symptoms.

Key words: gestational hypertension, preeclampsia, prediction, angiogenic factors, placental growth factor, fms-like tyrosine kinase-1

Introduction
High blood pressure during pregnancy is one of the leading causes of obstetric complications that increase the risk of morbidity and mortality among mothers and foetuses. According to the definition, gestational hypertension develops after 20th week of pregnancy. However, it is worth to mention, that the pathogenesis of this disorder begins at much earlier stages of pregnancy. Hypertension may result in a complication such a preeclampsia, a multi-organ disease manifested by proteinuria [1]. Despite well-known clinical risk factors (such as obesity, primogeniture and history of preeclampsia in multiparous pregnancies), there is still no established prediction method of the disorder.

The aetiology and pathogenesis of gestational hypertension and preeclampsia are not fully understood. Initial irregularities comprise the imbalance between placental pro-angiogenic and anti-angiogenic factors, while the target cells are maternal endothelial cells [2]. It is suggested that an important pathogenic role is played by soluble fms-like tyrosine kinase-1 (sFLT-1), vascular endothelial growth factor (VEGF), and placental growth factor (PIGF) [3].

At the beginning of the first trimester of a physiological pregnancy, the level of sFLT-1 concentration is more than ten times higher, and of PIGF – more than twice higher, when compared to non-pregnant women. In pregnancies that end in early miscarriage, both

1 The President Stanisław Wojciechowski University School of Sciences in Kalisz, Poland
2 Department of Perinatology and Gynecology, Poznań University of Medical Sciences, Poland
3 Laboratory of Environmental Research, Department of Toxicology, Poznań University of Medical Sciences, Poland
sFLT-1 and PI GF, measured between the sixth and tenth week, are much lower in comparison to pregnancies ending with live births [4]. After the first trimester, sFLT-1 remains constant while the concentration of PI GF increases until the end of the second trimester. In the last two months of pregnancy complicated by hypertension, the level of sFLT-1 increases in maternal blood, whereas the level of PI GF decreases [5]. These changes occur earlier and are more pronounced in women who will develop preeclampsia at a later stage of pregnancy [5]. In addition, the progress of these changes is greater in women who develop early-onset preeclampsia and in the cases where preeclampsia is accompanied by intrauterine foetal growth restriction [5]. Changes in the concentrations of sFLT-1 usually come a little later [6].

It is widely believed that these vasoactive substances may be promising biomarkers for prediction of preeclampsia in the first trimester of pregnancy. The ability to predict preeclampsia would be necessary to identify the women who would benefit most from early treatment, intensive monitoring and rapid interventions, if necessary. Treatment with low doses of aspirin, implemented before the 16th week of gestation, may effectively prevent or at least delay the early-onset of preeclampsia in women at high risk [7]. However, it has not been established yet, which women would benefit most from such treatment.

There is a theory that the analysis of PI GF and sFLT-1 concentrations could be useful in predicting preeclampsia. The main objective of our study was to assess the concentrations of sFLT-1 and PI GF as well as their ratio (sFLT-1/PI GF) in blood of pregnant women during each trimester of pregnancy in order to detect early gestational hypertension and preeclampsia before the onset of typical clinical symptoms.

Material and method

The project has been approved by the Bioethical Commission of the Poznań University of Medical Sciences (decision no. 539/09). The project has been funded by the National Science Centre – Kraków. The study included a random group of patients treated at the Outpatient Clinic of the Obstetrics Gynaecological Clinical Hospital of the Poznań University of Medical Sciences who signed written consent to take part in the study. The patients were selected for the study during an USG examination between 11+0 and 13+6 gw. The exclusion criteria included: multiple pregnancies, identified hypertension, endocrine disorders, diabetes, thrombophilia, inflammatory bowel disease and immune disorders diagnosed before pregnancy. In total, the study included 322 pregnant women. In three cases there was foetal death at a later stage of pregnancy; therefore, the final analysis included the remaining 319 patients. The women were divided into three groups: 0 – healthy, i.e. with normal blood pressure during the entire pregnancy (196; 61.4%) – control group; 1 – female patients who were diagnosed with gestational hypertension after 20 gw without significant proteinuria (107; 33.5%); 2 – female patients with hypertension and proteinuria > 300 mg/24 h – preeclampsia (16; 5.0%).

Gestation hypertension was defined as the occurrence of hypertension after the 20th week of gestation (systolic >140 mm Hg or diastolic >90 mm Hg) identified during two measurements conducted with the interval of 6 to 168 hours (1 week). Proteinuria was diagnosed in patients whose 24-hour urine protein concentration was higher than 300 mg. Patients with hypertension and proteinuria were diagnosed with preeclampsia.

In all patients, medical history, surveys, blood pressure measurements was taken and physical examinations as well as foetal ultrasound examination was performed. In majority of women Doppler uterine arteries blood flow examinations was performed.

Blood for biochemical tests was collected three times from the patients:

- 11 – 13 + 6 gw.
- 18 – 22 gw.
- 28 – 32 gw.

Blood samples were centrifuged and frozen at −80°C.

In each trimester of pregnancy, the concentration of placental growth factor (PI GF) and soluble fms-like tyrosine kinase 1 (sFLT-1) was assessed. Analysis was performed using reagents from Roche with the analyzer Cobas c 501 and e 601, while the results were presented in pg/ml units.

All patients were followed and treated at the hospital outpatient clinic or at the department of perinatology and gynaecology. The data regarding pregnancy period, complications and outcome was subsequently collected and analysed.

Analysis of statistics

The $\chi^2$ Pearson test or chi-square test with Yates correction was applied to examine statistical differences and to check the homogeneity of the groups. To compare concentrations of substances between the groups, Student's t-test was used, while to compare the sequential changes in the concentrations of PI GF and the sFLT-
1/PIGF ratio between the four groups, the non-parametric Kruskal-Wallis test was used. Mean values were compared using the variance analysis. The tested parameters were described with an arithmetic mean and standard deviation, as well as with minimal and maximal values. The value of $p < 0.05$ was considered to be statistically significant.

### Results

Table 1 presents the characteristics of individual groups. The concentration of sFLT-1 did not differ significantly between the groups in both the first and second trimester of pregnancy. In the third trimester, the concentration of sFLT-1 was significantly higher among patients suffering from gestational hypertension and in patients with preeclampsia when compared to healthy subjects ($p = 0.0047$) Table 1.

There was a significant increase in sFLT-1 concentrations between healthy patients and patients with hypertension, being the highest in patients who developed preeclampsia. Sequential changes in sFLT-1 concentrations between the groups increased in each group. The most significant increase of sFLT-1 concentration in all groups was observed in the second half of pregnancy. The greatest increase was found in women who developed preeclampsia, which was also statistically significant ($p = 0.002$).

In the control group, the concentration of PIGF was the highest when compared to other groups at each stage of pregnancy, while it was the lowest in patients with preeclampsia. In each trimester, differences in concentrations of this parameter between healthy patients and pregnant patients with preeclampsia were statistically significant. In the first trimester of pregnancy, significantly lower values of PIGF were found among women who were to develop preeclampsia in relation to other patients, both healthy women and women with hypertension without proteinuria (group 1).

### Table 1. Description of the studied groups

<table>
<thead>
<tr>
<th></th>
<th>Healthy pregnant women $(n = 196)$</th>
<th>Hypertension $(n = 107)$</th>
<th>PE $(n = 16)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (at time of enrolment) in years (SD)</td>
<td>31.1 (4.3)</td>
<td>30.3 (3.4)</td>
<td>28 (4.5)</td>
</tr>
<tr>
<td>Primaparity, n (%)</td>
<td>70 (35.9%)</td>
<td>33 (31.1%)</td>
<td>6 (40.0%)</td>
</tr>
<tr>
<td>Gestational age at childbirth (SD)</td>
<td>40.2 (1.3) **</td>
<td>39.8 (1.5) **</td>
<td>36.1 (2.6)</td>
</tr>
<tr>
<td>Fetal birth weight, g (SD)</td>
<td>3490 (450) **</td>
<td>3360 (430) **</td>
<td>2610 (490)</td>
</tr>
<tr>
<td>Gestational age at 1st sampling (SD)</td>
<td>12.4 (0.4)</td>
<td>12.8 (0.5)</td>
<td>12.0 (0.9)</td>
</tr>
<tr>
<td>Gestational age at 2nd sampling (SD)</td>
<td>20.3 (1.0)</td>
<td>20.2 (0.9)</td>
<td>19.6 (1.2)</td>
</tr>
<tr>
<td>Gestational age at 3rd sampling (SD)</td>
<td>29.6 (1.1)</td>
<td>29.4 (1.0)</td>
<td>28.3 (0.9)</td>
</tr>
</tbody>
</table>

*p < 0.05 between groups; **p < 0.05 when compared to patients with preeclampsia

### Table 2. Concentrations of sFlt-1, PIGF and sFlt-1/PIGF ratio in the studied groups

<table>
<thead>
<tr>
<th></th>
<th>Healthy pregnant women $(n = 196)$ (SD)</th>
<th>Gestational hypertension $(n = 107)$ (SD)</th>
<th>Preeclampsia $(n = 16)$ (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sFlt-1 (pg/ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 trimester</td>
<td>1766.9 (1537.6)</td>
<td>1784.9 (1991.0)</td>
<td>1896.6 (2635.5)</td>
</tr>
<tr>
<td>2 trimester</td>
<td>2443.6 (23969)</td>
<td>2303.1 (2396)</td>
<td>2025.7 (3488.2)</td>
</tr>
<tr>
<td>3 trimester</td>
<td>3783.0 (4071.5) **</td>
<td>5777.3 (6291.3) **</td>
<td>7856.3 (6171.3) **</td>
</tr>
<tr>
<td>PIGF (pg/ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 trimester</td>
<td>67.36 (92.7)*</td>
<td>68.26 (48.58) *</td>
<td>53.55 (23.43)</td>
</tr>
<tr>
<td>2 trimester</td>
<td>274.74 (245.9) **</td>
<td>212.65 (312.4) **</td>
<td>115.95 (484.3) **</td>
</tr>
<tr>
<td>3 trimester</td>
<td>451.69 (271.9) **</td>
<td>336.4 (213.5) **</td>
<td>220.0 (188.5) **</td>
</tr>
<tr>
<td>sFlt-1/PIGF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 trimester</td>
<td>33.71819*</td>
<td>33.62212*</td>
<td>43.40932</td>
</tr>
<tr>
<td>2 trimester</td>
<td>16.13632*</td>
<td>16.64078*</td>
<td>25.02582</td>
</tr>
<tr>
<td>3 trimester</td>
<td>30.77392 **</td>
<td>118.80942 **</td>
<td>172.23863 **</td>
</tr>
</tbody>
</table>

*p < 0.05 when compared to patients with preeclampsia; **p < 0.05 $p$ for multiple comparisons (bilateral)
sFlt-1: 1 trimester 2 trimester 3 trimester

- $p$ - ns
  - AUC = 0.55
  - 95% CI = 0.468–0.637
- $p$ - ns
  - AUC = 0.53
  - 95% CI = 0.448–0.618
- $p$ = 0.0007
  - AUC = 0.66
  - 95% CI = 0.575–0.739

PlGF: 1 trimester 2 trimester 3 trimester

- $p$ - ns
  - AUC = 0.52
  - 95% CI = 0.439–0.609
- $p$ < 0.05
  - AUC = 0.62
  - 95% CI = 0.532–0.697
- $p$ < 0.0001
  - AUC = 0.87
  - 95% CI = 0.802–0.921

sFlt-1/PlGF: 1 trimester 2 trimester 3 trimester

- $p$ - ns
  - AUC = 0.55
  - 95% CI = 0.436–0.632
- $p$ < 0.05
  - AUC = 0.60
  - 95% CI = 0.513–0.680
- $p$ < 0.0001
  - AUC = 0.87
  - 95% CI = 0.805–0.923

Fig 1. ROC curves in the prediction of hypertensive complications presenting the usefulness of sFLT-1 and PlGF (in $20 \pm 2$ gw and $30 \pm 2$ gw)

$p$ - ns – nonsignificant, AUC – area under curve, x – abscissa, y – ordinate)

At the subsequent stages of pregnancy, the differences in concentrations of PlGF increased significantly – the increase in concentration of this parameter was significantly higher among healthy women. Both in pregnant women with gestational hypertension and patients with preeclampsia the increase in the concentration of PlGF was significantly lower.

The sFLT/PIGF ratio was examined during the three trimesters of pregnancy. In all studied groups, the values of the parameter were relatively high in the first trimes-
ter, decreased in the second semester, and then increased substantially in the third trimester. The difference in this ratio between the first and second trimester of pregnancy was statistically significant only in the patients diagnosed with preeclampsia. In patients suffering from gestational hypertension and patients with preeclampsia a significant increase in the sFLT-1/PIGF ratio was observed in the period between the second and third trimester. The highest sFLT-1/PIGF values in each of these periods of pregnancy were observed among pregnant women who were diagnosed with preeclampsia at a later stage of pregnancy. In the first and second trimester, the ratio was significantly higher in patients with preeclampsia when compared to other patients (gr 0 vs. gr 2 and gr 1 vs. gr 2; \( p < 0.05 \)).

In the assays made in the third trimester, the differences gained significance also for multiple comparisons (Table 1).

To determine usability of the sFlt/PIGF ratio we used ROC – Receiver Operating Characteristics curves. It is a statistical tool used to assess test accuracy, showing the total description of the sensitivity and specificity of the test. The advantage of this method is that it shows the strength of the impact of a given factor on the occurrence of the event; in the analysed case – the risk of developing high blood pressure during pregnancy and preeclampsia.

The following charts present the ROC curves showing the applicability of the parameter for the assessment of the likelihood of hypertensive complications (gestational hypertension or preeclampsia).

The usefulness of both s-Flt-1 and PlGF evaluation in the first trimester of pregnancy has not been demonstrated. Also the constellation of sFLT-1/PIGF in early pregnancy turned out to have no significance for the prognosis of hypertensive complications.

The measurement of isolated sFlt-1 parameter (AUC = 0.66) during all stages of pregnancy turned out to be poor predictor of hypertensive complications. As pregnancy progressed, the concentration of PIGF was more useful in predicting hypertensive complications when compared to sFlt-1. Also the sFLT-1/PIGF ratio assayed in the second trimester was statistically significant for the prognosis of diseases associated with hypertension. In the test performed in the second trimester (between the 18th and 22nd week of gestation) the PIGF measured alone was slightly more sensitive when compared to the sFlt-1/PIGF ratio (AUC = 0.62 vs. AUC = 0.60). For the concentration of PIGF in the second trimester of pregnancy a value smaller than 349.3 pg/ml was associated with the risk of hypertensive complications with 52.8% sensitivity and 67.9% specificity – so not being satisfactory parameter. The value of the sFlt-1/PIGF ratio higher than 5.59 was associated with the occurrence of hypertension with 49.4% sensitivity of and 75.4% specificity (Fig. 1).

At a later stage of pregnancy (30 ± 2 gw), a comparable sensitivity level in the prediction of hypertension could only be attributed by measuring the sFlt-1/PIGF ratio (AUC = 0.87) or PIGF alone (AUC = 0.87). The concentration of PIGF in the third trimester of pregnancy of less than 94.03 pg/ml was associated with a higher risk of hypertensive (87.2% sensitivity and 77.3% specificity). The cut-off point for the sFlt-1/PIGF ratio was 38.9; higher values were associated with the risk of hypertension (83.5% sensitivity and 90.7% specificity) (Fig. 1).

**Discussion**

The presented clinical study was conducted among women who were under the care of perinatal outpatient clinic at a third degree reference centre. Under the care of this outpatient clinic are patients with initially greater risk of such complications, often chronically ill, with a history of obstetric problems as well as older patients when compared to the general population. It should be emphasized that the presented results may be slightly different from the results presented in the literature due to the specific place of recruitment of the patients.

The study presented by us is in accordance with the majority of available publications, tried to find significant differences in the concentration of sFLT-1 in the first half of pregnancy among women who developed late-onset of preeclampsia when compared to physiological pregnancies [8, 9]. We have not demonstrated the usefulness of presented parameter in prediction of hypertension and preeclampsia in the first and second trimester. Significant changes in the concentration of this parameter were recorded only in 30 ± 2 gw. However, there are available studies showing elevated levels of sFLT-1 starting from the 13th week of gestation [10, 11]. Vatten et al. [12] studied 154 women who developed preeclampsia before 37th week of pregnancy, 190 women who developed preeclampsia after 37th week and 392 women in the control group. They found that the sequential change in the concentration of sFLT-1 between the first and second trimester has a strong predictive power in the prediction of preeclampsia. The earlier the symptoms appeared, the stronger the increase in the concentration of FLT-1 was observed between the first
and second trimester. Villa et al. observed elevated sFLT-1 levels between the 12th and 14th week of pregnancy in women who developed a late onset preeclampsia or gave birth prematurely [6, 9, 14, 15]. Cowans et al. [16] and Noori et al. [17] demonstrated significantly reduced levels of PI GF starting in the first trimester of pregnancies following early-onset of preeclampsia. In the group of patients we have studied, we did not observe any differences in the concentrations of PI GF in the first trimester; however, we recorded reduced values of this parameter in the second sampling (20 ± 2 gw) among patients with hypertension, in particular among patients with preeclampsia. Our study indicated that during the stage of the second trimester of pregnancy it is possible to distinguish patients with exceptionally high risk of these complications several weeks before the diagnosis is made. A decreased PI GF value in 20 ± 2 gw could indicate the development of hypertensive complications with AUC 62% (PPV 70% and NPV 88%). In the course of pregnancy, the parameter increased its prognostic value in predicting hypertensive complications in the studied population so that in 30 ± 2 gw AUC reached 87% (PPV 83%, NPV 90%).

Previous studies have shown that the sFLT-1/PI GF ratio is a better predictor of preeclampsia compared to the evaluation of sFLT-1 or PI GF alone [10]. In our study, the analysis of isolated PI GF in the second trimester of pregnancy was a better predictor of hypertensive complications compared to s-Flt1/PI GF (AUC = 62% vs. AUC = 60%). We have demonstrated that in the period between the 18th and 22nd gw a lower concentration of PI GF (< 349.3 pg/ml) in the serum of women and the sFLT-1/PI GF ratio higher than 5.59 were associated with an increased risk of hypertensive complications at a later stage of pregnancy. Emphasis should be placed on the relatively low sensitivity of 52.8% and specificity of 67.9% of PI GF as well as of the sFLT-1/PI GF ratio (49.4% sensitivity and 75.4% specificity). In the study by Levine et al., the sFLT-1/PI GF ratio was significantly higher already from the 17th to 20th week of pregnancy in women who later developed preeclampsia [3]. Moore Simas et al. have shown that the ratio of sFLT-1/PI GF calculated in 22-26 gw showed a strong prediction in women with early-onset preeclampsia [8].

In our study, the greatest differences in the concentrations of all the tested parameters were obtained in evaluations performed in the third trimester of pregnancy (30 ± 2 gw). The women at risk of hypertension demonstrated significantly higher concentrations of s-Flt-1 (> 3712 pg/ml) and significantly lower values of PI GF (< 94.03 pg/ml). The concentration quotient of sFLT-1/PI GF higher than 38.9 significantly increased the risk of hypertension in pregnancy. The prognostic value of the sFLT-1/PI GF ratio has increased in 30 ± 2 gw (AUC 87%). Villa et al. evaluated the risk of preeclampsia. As in our study, they also observed a higher value of both PI GF and sFLT-1/PI GF ratio when assessed at later stages of pregnancy. In that group, the sFLT-1/PI GF ratio was AUC 100% for early-onset preeclampsia [13]. In the study by Moore Simas et al., elevated values of the studied parameters were observed at a later stage (between the 25th and 30th week) of pregnancy in the group of pregnant women who developed late-onset preeclampsia (after the 34th week) [8]. In our study, all the women who developed preeclampsia showed elevated values of the sFLT-1/PI GF ratio in the last blood sampling (30 ± 2 gw), which was about 3.5 to 6.4 weeks before the diagnosis of preeclampsia. Which means that theoretically, we were able to identify patients about one month before the appropriate, clinical diagnosis. From a clinical point of view, these results may be important in helping obstetricians to decide on the treatment of women in a high-risk group. Adequate knowledge gives time to consider the method and intensity of monitoring of the patient and the foetus, to decide if hospitalization is justified, to transfer the patient to a more specialized centre, and sometimes – to decide on an early termination of pregnancy.

Moore Simas et al. analysed the sFLT-1/PI GF ratio in patients suffering only from hypertension without proteinuria. They found no significant differences in the parameter between women who developed only hypertension as compared to the healthy control group at all stages of gestation [8]. In our study, we observed a significant increase in the sFLT-1/PI GF ratio in patients with gestational hypertension compared to the control group only in the third trimester (30 ± 2 gw). Moreover, this parameter was significantly more elevated in the women with preeclampsia.
Interestingly, the ratio of sFLT-1/PlGF proposed by Verlohren et al. can be useful not only as a predictor of preeclampsia but also in the differential diagnosis of diseases associated with hypertension in pregnancy in female patients exposed to an increased risk (at least one clinical risk factor for preeclampsia: a history of hypertensive disease in previous pregnancies, obesity BMI > 30, elevated pulsatility index in the uterine arteries as well as patients suffering from chronic hypertension) [19, 20]. These authors believe that the sFLT-1/PlGF ratio can serve as a predictor of preeclampsia and as a predictor of the severity of this disease in patients already diagnosed with preeclampsia [19, 20]. Verlohren et al. suggests that the value of sFLT-1/PlGF ratio should be used for individual risk stratification in patients who have had preeclampsia in previous pregnancies [20]. Rana et al. [10] studied the levels of angiogenic factors in women with a clinical suspicion of preeclampsia, and found that in women with early-onset preeclampsia (< 34 weeks) increased values of the sFLT-1/PlGF ratio were observed two weeks before the start of clinical symptoms. They showed an inverse correlation between the sFLT-1/PlGF ratio and the duration of pregnancy in terms of the severity of preeclampsia [10].

Vasoactive substances can be different in the cases without proteinuria and with proteinuria, in early- and late-onset preeclampsia; moreover, differences may be observed in cases of more or less aggressive course of the disease. All of this may reflect differences in the pathogenesis of subtypes of hypertension associated with pregnancy and preeclampsia. Early-onset preeclampsia is considered to be more of a placenta disease arising due to improper placentation and it often shows familial predisposition suggesting a genetic disease and a high risk of recurrence. On the other hand, late-onset preeclampsia is seen more as a maternal illness. Early-onset preeclampsia is often associated with a placenta failure; also, it frequently leads to limitation of foetus growth. The late-onset disease emerges from maternal predisposing risk factors, such as metabolic factors associated with obesity, chronic hypertension, diabetes, and interaction with normal placenta [21].

Our study is an attempt to prospectively indicate the variation in angiogenic factors concentrations in women at high risk. While analysing them, one must remember that the main objective was to assess the concentrations of selected parameters among patients with hypertensive complications. A limitation in our study was the relatively small group of patients with preeclampsia, as well as the lack of separation of the two types of preeclampsia, namely the so-called early- and late-onset disease. This was due to the fact that in the group of 16 patients with preeclampsia only 4 have developed so-called early-onset preeclampsia. One should bear in mind the fact that the proportion of women with early-onset preeclampsia in relation to the late form of the disease was similar to that typically observed in clinical practice, which is why it was decided to analyse them together.

To sum up, more prospective studies are required to determine whether these biomarkers may be useful in predicting the imminent appearance of clinical symptoms of hypertensive diseases, thus being suitable for application in clinical practice.

References


M. Chuchracki
President Stanisław Wojciechowski
University School of Sciences in Kalisz
Nowy Świat 4, 62-800 Kalisz, Poland
e-mail: mchuch@wp.pl