Basic principles and structure of risk assessment of Great obstetrical syndromes

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The objective: to develop a method for predicting the individual risk for great obstetric syndromes (GOS).

Materials and methods. An analysis of the somatic, reproductive, and obstetric anamnesis was conducted in 572 pregnant women with clinical manifestations of GOS, in 81 of them (prediction group) signs of placental dysfunction were detected based on clinical, functional, laboratory, and ultrasound data. Control group (CG) – 50 practically healthy pregnant women with a favorable reproductive history and an uncomplicated course of this pregnancy.

Functional, biophysical, hormonal, immunological and hemocoagulation indicators were calculated to determine the informative (prognostic) significance. Quantitative signs were divided into diagnostic intervals, and qualitative signs were assigned a code. The following indicators were included in the standard protocol: age, data on somatic and gynecological history, data on the pregnancy course, results of functional and laboratory examinations. Statistical processing of research results was carried out using standard Microsoft Excel 5.0 and Statistica 6.0 programs.

Results. In the I trimester of pregnancy the concentration of placental lactogen (PL) in the prediction group was 29.4 % lower than the CG indicator, estradiol (E_2) amount – by 27.4 %, estriol (E_3) – by 28.6 %, progesterone (PG) – by 34.4%, human chorionic gonadotropin (hCG) – by 28.3 % lower, and cortisol (CR) – by 36.1 % higher. At the beginning of the II trimester of pregnancy in the prediction group the level of PL was already reduced by 33.8 %, E_2 – by 26.2 %, E3 – by 32.3 %, PG – by 37.4 %, hCG – by 30.6 %, and CR – increased by 43.6 % compared to CG.

The indicators of placenta hormonal activity in the early stages of pregnancy and at the beginning of the II trimester can be prognostic signs of further disruption of the adaptive compensatory and adaptive reactions of the fetal placental complex (FPC) in the II and III trimesters of pregnancy. Among a wide range of hemostasiological indicators in the I trimester of pregnancy in the prediction group the most informative were: activated partial thromboplastin time (-23 %) and activated recalcification time (+16.2 %), the changes of which remained at the beginning of the II trimester (-40% and - 11.7% respectively).

During the evaluation of thromboelastogram data, the value of "r+k" was fixed by 33.3 % lower in the I trimester and by 36 % – at the beginning of the II trimester of pregnancy. As a result of the analysis the indicators with a high information value (more than 3.0 c.u.) were selected for quantitative assessment of the degree of individual risk for the development of maladaptive disorders in the FPC. The clinical trial of the scoring method of prediction proved its high sensitivity (91.8 %) and specificity (85.6 %).

Conclusions. A multi-faceted analysis of anamnestic data, features of the pregnancy course, basic clinical, laboratory and functional indicators in women with clinical manifestations of GOS made possible to develop an effective methodology for predicting the risk for GOS development with high levels of sensitivity and specificity.

Keywords: *somatic anamnesis, reproductive anamnesis, obstetric anamnesis, great obstetric syndromes, development forecasting, informative prognostic criteria.*

Основні принципи і структура оцінювання ступеня ризику розвитку великих акушерських синдромів
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Мета дослідження: розроблення методу прогнозування індивідуального ризику розвитку великих акушерських синдромів (ВАС).

Матеріали та методи. Проведено аналіз соматичного, репродуктивного, акушерського анамнезу у 572 вагітних із клінічними проявами ВАС, у 81 (група прогнозування) з яких на підставі клініко-функціональних, лабораторних, ультразвукових даних були виявлені ознаки плацентарної дисфункції. Контрольна група (КГ) – 50 практично здорових вагітних зі сприятливим репродуктивним анамнезом і неускладненим перебігом даної вагітності.

Для визначення інформаційної (прогностичної) значущості обраховано функціональні, біофізичні, гормональні, імунологічні та гемокоагуляційні показники. Кількісні ознаки були розділені на діагностичні інтервали, а якісним ознакам присвоювали код. До стандартного протоколу включали такі показники: вік, дані соматичного та гінекологічного анамнезу, дані перебігу вагітності, результати функціональних та лабораторних обстежень. Статистичне оброблення результатів досліджень проводили з використанням стандартних програм Microsoft Excel 5.0 та Statistica 6.0.

Результати. У I триместрі гестації концентрація плацентарного лактогену (ПЛ) у групі прогнозування була на 29,4 % меншою щодо показника КГ, естрадіолу (E_2) – на 27,4 %, естріолу (E_3) – на 28,6 %, прогестерону (Пг) – на 34,4 %, хоріонічного гонадотропіну людини (ХГЛ) – на 28,3 % нижчою, а кортизолу (Кр) – на 36,1 % більшою. На початку II триместра вагітності у групі прогнозування рівень ПЛ був зменшений вже на 33,8 %, E_2 – на 26,2 %, E_3 – на 32,3 %, Пг – на 37,4 %, ХГЛ – на 30,6 %, а Кр – збільшений на 43,6 % порівняно з КГ.

ГІНЕКОЛОГІЯ

Показники гормональної активності плаценти у ранні терміни гестації і на початку II триместра можуть бути прогностичними ознаками подальшого зриву адаптаційних компенсаторно-пристосувальних реакцій фетоплацентарного комплексу (ФПК) у II і III триместрах вагітності. Серед широкого спектра гемостазіологічних показників у I триместрі вагітності у групі прогнозування найбільш інформативними виявились: активований частковий тромбопластиновий час (-23 %) та активований час рекальцифікації (+16,2 %), що збереглося й на початку II триместра (-40 % та -11,7 % відповідно).

Під час оцінювання даних тромбоеластограми значення "r+k" фіксували на 33,3 % меншим у I триместрі та на 36 % – на початку II триместра вагітності. У результаті проведеного аналізу були виділені показники з високою інформаційною цінністю (більше 3,0 у.о.) для кількісної оцінки ступеня індивідуального ризику розвитку дезадаптаційних порушень у ФПК. Клінічне випробування бального методу прогнозування засвідчило його високу чутливість (91,8 %) та специфічність (85,6 %).

Висновки. Багатоаспектний аналіз анамнестичних даних, особливостей перебігу вагітності, основних клініко-лабораторних і функціональних показників у жінок із клінічними проявами ВАС дозволив розробити ефективну методику прогнозування ризику розвитку ВАС з високими рівнями чутливості та специфічності.

Ключові слова: *соматичний анамнез, репродуктивний анамнез, акушерський анамнез, великі акушерські синдроми, прогнозування розвитку, інформаційні прогностичні критерії.*

The main characteristics of the GOS are [1, 2]: multi etiology; prolonged preclinical stage; frequent fetal involvement; adaptive nature of clinical manifestations. The development of syndromes is the result of complex interactions between maternal and fetal genomes and the environment [5–9]. The following conditions are classified as GOS: preterm birth; premature rupture of membranes; preeclampsia; fetal growth retardation; macrosomia; missed abortion; stillbirth; spontaneous abortion; placental abruption [10–20].

Recently, there have been publications about gestational diabetes (GDM) as one of the GOS [22]. It is established that the impact on the fetus and complications of the neonatal period is a consequence of metabolism projected to the fetus through the placental interface. Therefore, GD can be considered one of the GOS. GOS is characterized by systemic inflammation, endothelial dysfunction, increased thrombin production, predominance of antiangiogenic factors and often leads to damage to many organs and systems [22]. According to the data published in 2011 by scientists I. Brosens and co., the basis of GOS is the pathology of the so-called deep placentation [23].

In preeclampsia, only a small part of the spiral arteries in the center of the placental site may show signs of complete transformation of the zone with connection of the myometrial segment. Additionally, arterial obstruction (e.g. thrombosis, acute atherosclerosis) can lead to or determine the severity of defective placentation. Disruption of placentation («defective placentation») with early rupture together with limited invasion of the spiral arteries by extravillous trophoblast leads to impaired remodeling and may cause early development of preeclampsia, which is often combined with Fetal growth retardation (FGR) or FGR without preeclampsia [22, 23].

The development of perinatology as a science of the fetus and infant, determination of the main parameters of normal and disturbed homeostasis of the fetoplacental complex with the subsequent development of methods for predicting and correcting the identified disorders is an important reserve for reducing obstetric and perinatal pathology, neonatal morbidity and mortality. This determines not only medical but also social importance and relevance of the study of the main fetal life support system – the fetoplacental complex, which integrates numerous relationships between the fetus and the mother [6, 24].

The deterioration of the ecological situation, irrational nutrition, bad habits in combination with chronic diseases in pregnant women and the use of medications without taking into account their possible impact on placental homeostasis, leads to the development of placental dysfunction syndrome, which, in turn, is the cause of numerous disorders in the functional system of mother-placenta-fetus. Placental insufficiency, caused by disorders of its adaptive and homeostatic reactions, is either a complication associated with the pathological course of pregnancy against the background of extragenital pathology, or an independent nosological unit.

Much evidence links placental vascular pathology with poor fetal growth and adverse pregnancy and delivery. And in turn, endothelial dysfunction and defective deep placentation are the basis for the development of great obstetrical complications (GOS) or placenta-associated diseases of pregnancy [22, 23].

The search for effective methods of predicting GOS is ongoing in order to correct the disorders early and reduce the negative consequences for the mother and fetus. Despite the sufficient study of the problem, there is still no single point of view on the peculiarities of the pathogenesis of disorders of the functional state of the fetoplacental complex, which are the basis for the development of GOS, no unified methodological approaches to early diagnosis have been developed, and there are no standards for the examination and treatment of pregnant women with identified disorders [5–9]. Therefore, the development of an effective methodology for predicting the development of «great obstetrical syndromes» becomes relevant and timely.

The objective: is to develop a method for predicting the individual risk of developing great obstetrical syndromes.

MATERIALS AND METHODS

To develop an effective system for predicting GOS, we prospectively analyzed 572 deliveries at the maternity hospital in Uzhhorod in 2021, 81 of which had signs of placental dysfunction based on clinical, functional, laboratory, ultrasound examinations. We called this group the "prediction group" because, based on the identified risk factors for the development of GOS, we have developed a methodology for predicting the development of GOS. Control group (CG) – 50 practically healthy pregnant women with a good reproductive history and uncomplicated course of this pregnancy.

To develop a medical algorithm for determining the degree of individual risk of developing GOS, two main tasks were set: - to identify the statistical dependence of the indicators of clinical, laboratory and instrumental methods of examination in pregnant women of this group on the existing clinical manifestations of GOS; – to develop a method for predicting the degree of individual risk of GOS, using highly effective information and prognostic criteria.

To determine the informational (prognostic) significance, we selected functional, biophysical, hormonal, immunological and hemocoagulation parameters. History data, the results of clinical, laboratory and instrumental research methods were recorded in a specially designed formalized card. At the same time, quantitative features were divided into diagnostic intervals, and qualitative features were assigned a code. The standard protocol included the following indicators: age, data of somatic and gynecological anamnesis, factors characterizing the course of this pregnancy, results of functional and laboratory examinations. Statistical processing of the research results was performed using standard Microsoft Excel 5.0 and Statistica 6.0 programs [25, 26].

RESEARCH RESULTS AND THEIR DISCUSSION

Practice shows that even a detailed clinical assessment of risk factors for the development of GOS, in combination with conventional obstetric examination methods, allows to detect the initial forms of placental insufficiency in no more than 1/3 of pregnant women. The most commonly used method of diagnosing disorders in the placental complex, at present, is ultrasound, which is widely used
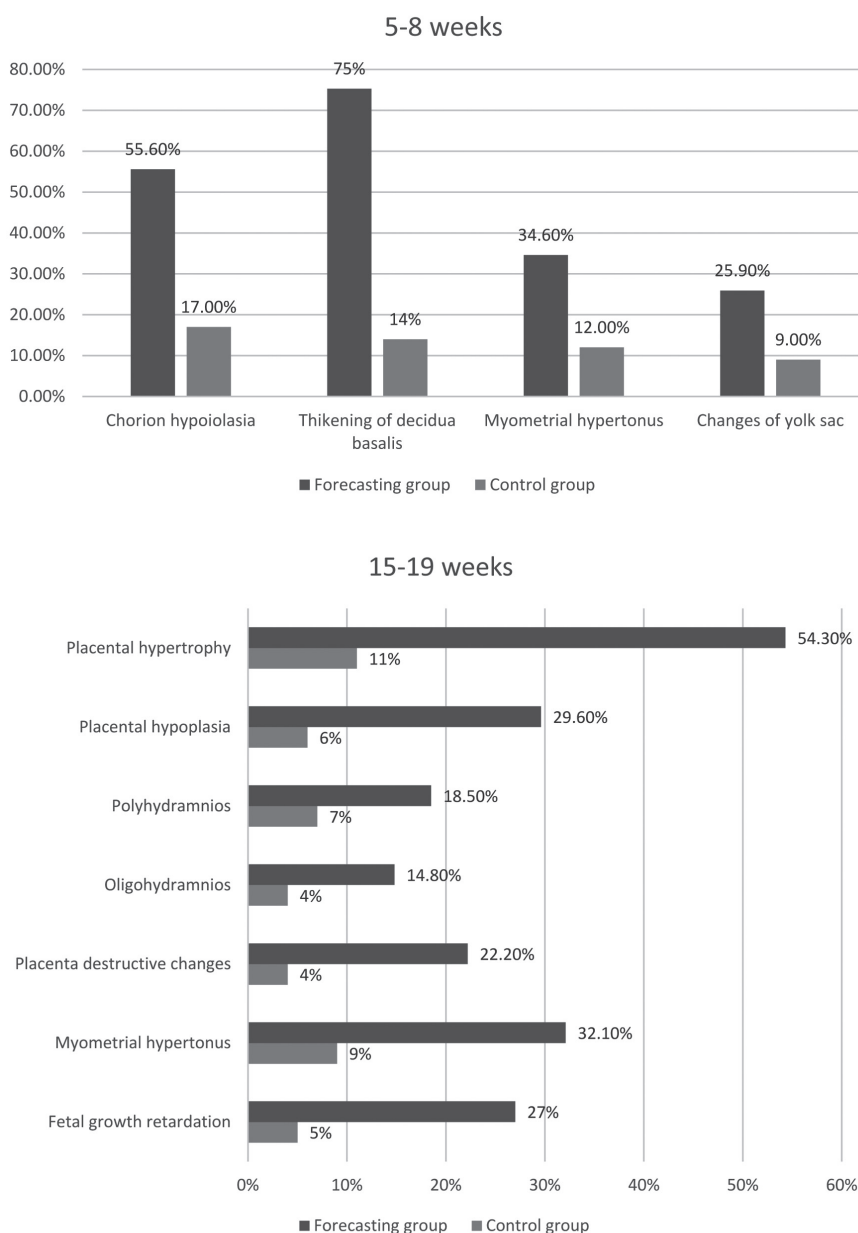

5-8 weeks

15-19 weeks

Fig. 1. Ultrasound features of the fetoplacental complex (%)

in practical health care and has a great screening capacity. A scientifically based program of ultrasound examination of pregnant women, which has become quite widespread in all regions of Ukraine, has as its main goal the detection of, first of all, congenital malformations of the fetus [3].

However, in modern conditions, there is every reason to more widely practice serial ultrasound aimed at diagnosing placental insufficiency. As the generalization of the literature data and our own clinical experience shows, for the prognosis and early diagnosis of disorders in the FPK, it is advisable to start the study in the first trimester of pregnancy from 5–8 weeks, at the beginning of the second trimester – at 15–19 weeks, and repeated ultrasound – at 24–27 and 33–36 weeks of gestation. Such an ultrasound monitoring program makes it possible to timely detect at least 80% of violations.

Ultrasound examination of women of the prediction group, compared with the control group of pregnant women, in the first trimester of gestation (5–8 weeks) revealed a number of features during the formation of the fetoplacental complex (Fig. 1). Hypoplasia of the chorion was diagnosed in 55.6% (17%), thickening of the decidua basalis – in 75.3% (14%), hypertension of the myometrium – 34.6% (12%), changes in the yolk sac – 25.9% (9%) of observations. At the beginning of the second trimester of pregnancy (15–19 weeks), placental hypertrophy was detected in 54.3% (11%) of cases, placental hypoplasia – in 29.6% (6%), hyperhydramnios – in 18.5% (7%), anemia - in 14.8% (4%), destructive changes of the placenta were diagnosed in 22.2% (4%), myometrial hypertension – in 32.1% (9%), GDM (delayed fetal growth) occurred in 27.2% (5%) of cases.

The development of maladaptive disorders in the placenta is characterized by the presence of higher ultrasound density, the degree of which reflects the severity of involutional morphological changes in the placenta. We determined the structural integrity of the placenta at the beginning of the second trimester of gestation in points using the Kozlowki scale. According to the data obtained, there is an increase in this indicator in pregnant women of the prognosis group compared to the control (5 points vs. 4 points, respectively).

Thus, the results of ultrasound examination of the features of the formation of the placenta previa in the first trimester and its condition at the beginning of the second trimester of pregnancy allow us to conclude about their diagnostic value in relation to the prediction of maladaptive disorders in the mother-placenta-fetus system, starting from early gestation. With pronounced echographic signs of disorders of the formation of the placenta previa, one can assume a further delay in the development of the placenta.

Doppler indices (increase in RI and PI) are signs of obvious maladaptation disorders in the mother-placenta-fetus system, which appear in the third trimester of pregnancy and, according to the literature and our own observations, are evidence of an existing placenta insufficiency, and therefore, in our opinion, cannot be an independent information and prognostic criterion.

Changes in the hormonal function of the fetoplacental complex are easily quantified and can be an affordable prognostic test for detecting disorders in the mother-placenta-fetus system. For this purpose, in the examined pregnant women of the prognosis group, we determined the percentage deviation of the levels of hormones of the FPC, in relation to the CG, as the most informative markers of hormonal regulation of the placenta. Thus, according to the data obtained (Fig. 2), in the first trimester of gestation, the concentration of PL (placental lactogen) in the prediction group was 29.4%, E_2 (estradiol) – 27.4%, E_3 (estriol) – 28.6%, Pg (progesterone) – 34.4%, hCG (human chorionic gonadotropin) – 28.3% lower, and CR (cortisol) – 36.1% higher, relative to the CG.

At the beginning of the II trimester of pregnancy, the level of PL was already reduced by 33.8%, E_2 – by 26.2%, E_3 – by 32.3%, Pg – by 37.4%, hCG – by 30.6%, and Cr –
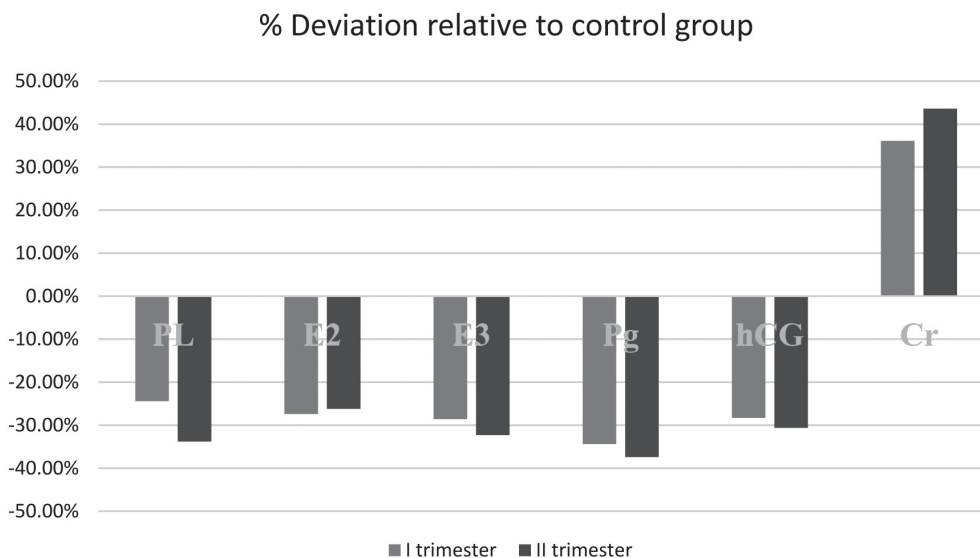

% Deviation relative to control group

Fig. 2. Changes in the hormonal function of the FPC in women of the prognosis group
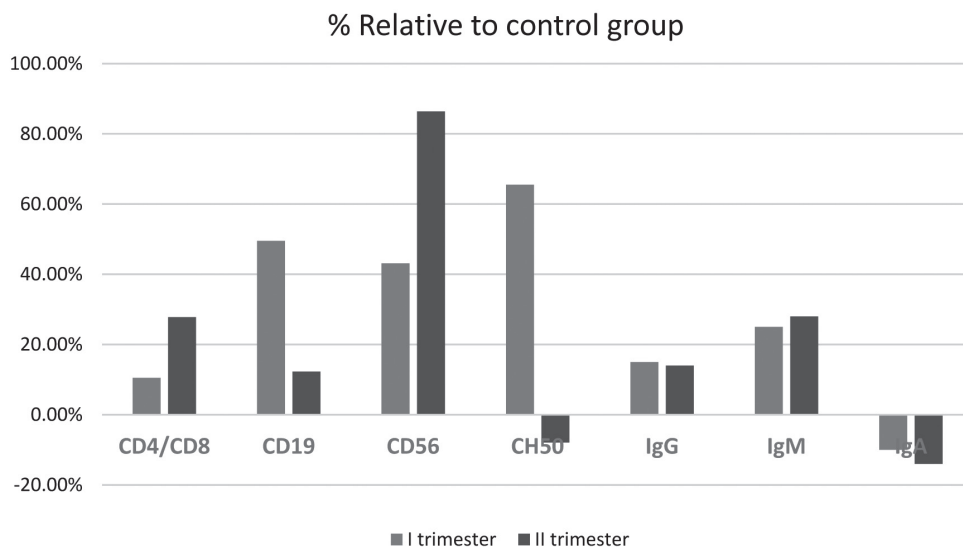
% Relative to control group

Fig. 3. Changes in systemic immunity in women of the prognosis group

increased by 43.6%. The differences between the groups in all cases were significant (p<0.05). That is, indicators of hormonal activity of the placenta in early gestation and early II trimester may be prognostic signs of further disruption of adaptive compensatory and adaptive reactions of the placenta in the II and III trimesters of pregnancy.

The immune system is one of the main systems that ensure the homeostasis of the body. Since there is a direct correlation between the functional capacity of the forming fetoplacental complex and the state of the immune response, in particular to trophoblast antigens, we conducted research in this direction to identify possible prognostic immunological criteria. The main changes in systemic immunity in pregnant women with CG are shown in Fig. 3.

The following features were found in the prognostic group compared to the CG: an increase in the immunoregulatory index (CD4+ / CD8+) by 10.5% in the first trimester and by 27.8% at the beginning of the second trimester, the content of B-lymphocytes (CD19+) was increased by 49.5% in the first trimester and by 12.3% at the beginning of the second trimester, the level of natural killer cells (CD56+) – by 43,1% in the first trimester and 86.4% at the beginning of the second trimester, the index of hemolytic activity of the classical pathway of complement activation (CH$_{50}$) in the first trimester increased by 65.5%, but at the beginning of the second trimester of pregnancy was reduced by 7.9%.

The level of immunoglobulins was as follows: in the first trimester in the prognosis group, relative to the CG of pregnant women, the level of IgG and IgM was higher by 15% and 25%, respectively, the level of IgA was lower by 10%, at the beginning of the second trimester of pregnancy, the level of IgG and IgM was higher by 14% and 28%, respectively, and the level of IgA decreased by 14%. In this regard, in our opinion, it is possible to conclude that it is advisable to include the above-mentioned indicators of immune status in the system for predicting the risk of developing GOS.

Taking into account, known from the literature [7, 9, 13], the relationship of the severity of placental insufficiency and fetal growth retardation syndrome (FGR) with the state of rheological and aggregation properties of blood, we studied hemocoagulation parameters in pregnant women of the prognosis group in order to identify prognostic signs of the risk of developing maladaptive disorders in the FPC. The dynamics of changes in hemocoagulation parameters in the I and early II trimester, relative to the CG, is shown in Fig. 4. Among a wide range of hemostasiological parameters in the first trimester of pregnancy in the prognosis group the most informative were Activated partial thromboplastin time (APTT) (-23%) and activated recalcification time (ART) (+16.2%), which remained at the beginning of the second trimester (-40% and -11.7%, respectively). When evaluating the thromboelastogram data, the value of «r + k» was 33.3% lower in the first trimester and 36% - at the beginning of the second trimester of pregnancy. At the same time, the value of «ma» – on the contrary, increased in the first trimester by 20.8% and 11.4% – at the beginning of the second trimester. TPI was almost 2 times higher in women of the prognosis group in the I trimester and early II trimester compared to the control group.

The concentration of FFDP in pregnant women of the prognostic group in the first trimester was 3.7 times higher, and at the beginning of the second trimester - 3.9 times higher than in the control group. Particular attention should be paid to the level of stable metabolites of prostacyclin – 6-keto-PgF$_1$ and thromboxane - TxB$_2$. The concentration of the first was 46.5% lower, and the second - 74.7% higher, relative to the control group already in the first trimester of pregnancy. Thus, the ratio of 6-keto-PgF$_{1\alpha}$/TxB$_2$ in the first trimester in the prognostic group was 3.3 times higher.

Thus, the comparison of indicators of hemostasis in pregnant women of the prognosis group, compared with the CG, made it possible to identify some of them that can be used as prognostic criteria for the risk of developing maladaptive disorders in the mother-placenta-fetus system.
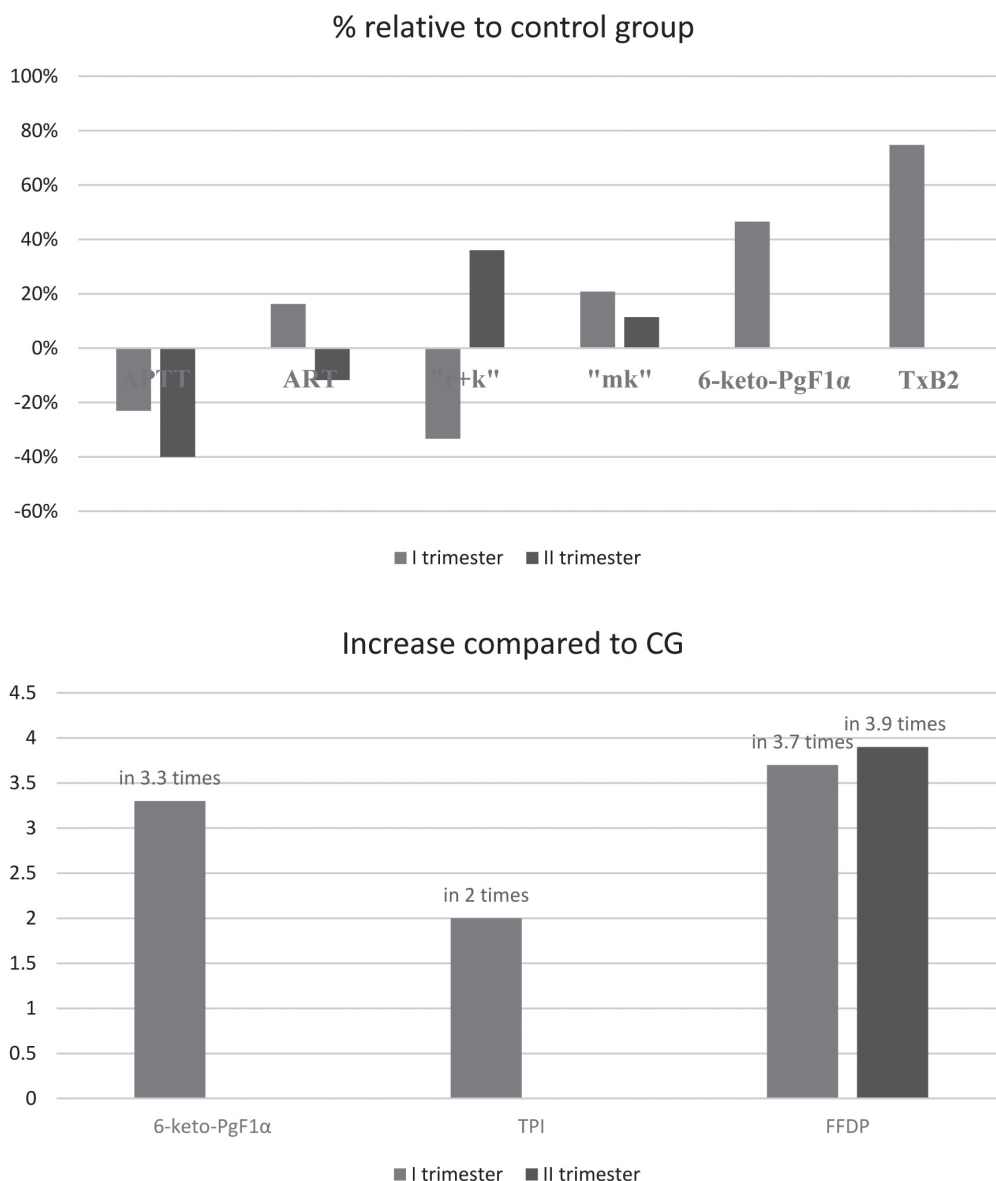
% relative to control group

■ I trimester ■ II trimester

Increase compared to CG

■ I trimester ■ II trimester

Fig. 4. Dynamics of changes in hemocoagulation parameters in women of the prognosis group

To create a system for predicting maladaptive disorders in the fetoplacental complex in women of the prediction group, we used a sequential recognition procedure based on the Bayesian method as the basis for mathematical modeling. The theoretical basis of this method is based on the theory of pattern recognition. When using a small number of features (no more than 10), the probability of a relationship between those features is small, but increasing the number of features leads to a significant increase in the probability of a relationship between them, which greatly reduces the accuracy of the modeling. Also, the diagnostic information inherent in the combined variants of traits is completely cut off.

As an indicator of the relationship between them, Pearson's pairwise correlation coefficient is used. In total, about 40000 correlation coefficients were invented. Highly correlated were considered the traits whose pairwise correlation coefficient was greater than 0.6. As a result, 8 groups of highly correlated features were identified, which were the basis of our forecasting methodology.

Thus, the analysis of our statistical data allowed to significantly reduce the number of features that do not have significant differences to assess the degree of individual risk of maladaptation disorders in the fetoplacental complex. The main groups of the most informative features are presented in Table 1.

This table presents the statistically processed data (calculations of the likelihood ratio and the prognostic coefficient, as well as the informative value of the trait) in women of the forecasting group. As a result of the analysis, we have identified indicators with «high» information value (more than 3.0 units) to quantify the degree of individual risk of developing maladaptive disorders in the FPC.

Table 1

Information value of signs and prognostic coefficients for assessing the degree of individual risk of maladaptation disorders in the mother-placenta-fetus system in women with EAC

Name of the features	The ratio of the difference of features	Predictive coefficient	Information value of the feature
Age:			
- up to 20 years	2,11	3,72	2,09
- from 21 to 35 years old	1,21	-0,81	0,41
- more than 35 years	2,01	3,60	2,06
Gynecological pathology:			
- menstrual dysfunction	2,0	3,60	1,71
- chronic adnexitis	2,04	3,62	1,84
- polycystic ovary disease	1,31	1,10	0,26
Extragenital pathology:			
- arterial hypertension	1,75	2,21	0,83
- pyelonephritis	2,85	4,50	2,47
- thyroid pathology	4,25	5,82	4,75
- anaemia	1,50	2,01	1,62
Complications of this pregnancy in the first trimester:			
- threatened misscarriage	2,75	4,20	4,25
- anaemia	3,21	5,22	3,16
First trimester ultrasound:			
- chorion hypoplasia	2,20	3,41	2,38
- thickening «decidua basalis»	2,04	3,62	1,84
- hypertension of the myometrium	1,53	1,82	1,83
- changes in the yolk sac	1,30	1,10	0,77
Second trimester ultrasound:			
- placental hypertrophy	2,30	3,20	4,56
- placental hypoplasia	2,85	4,30	2,47
- polyhydramnios	2,0	3,10	1,84
- oligohydramnios	2,50	4,02	2,62
- hypertension of the myometrium	2,0	3,60	2,06
- destructive changes in the placenta	2,2	3,2	2,16
- fetal retardation	5,25	6,2	5,6
- change in placental structure (P. Kozlowki scale) > 4 points	1,5	1,8	1,8
Endocrine status I trimester:			
- E_3 <30%	2,2	3,4	2,38
-HCG< 30%	2,5	3,9	2,79
-Pg <35%	1,5	1,8	1,8
-PL <30%	2,6	3,6	1,86
- Cr >30%	2,5	4,0	2,6
II trimester:			
- Pg <40	2,0	3,6	1,71
- PL <40%	2,75	4,2	2,4
- E_3 <40%	2,85	4,5	2,47
- Cr >40%	3,2	5,3	3,64
Changes in systemic immunity I trimester:			
- CD4+/CD8+ >2	3,8	5,2	3,6
- CD19+ >25%	1,72	2,31	1,68
- CD56+ > 25%	3,6	5,0	3,4
- SN50 >30%	2,2	4,6	2,4
- IgG >10%	1,82	2,62	2,96
- IgM >20%	1,89	2,60	4,03
- IgA <10%	1,82	2,62	2,96
AFA:			
- available	2,75	4,2	1,83
- missing	1,20	-0,80	0,72
Changes in hemostasis I trimester:			
- APTT< 30 sec	2,0	3,6	1,84
- ART >70 sec.	2,4	3,8	3,02
- TPI>20 c.u.	3,0	4,2	2,8
- FFDP >2x10 g/l	2,2	3,4	2,38
- PgI_2 /TxA_2 <0.8	2,75	4,2	4,25

Among a wide range of anamnestic data, the most significant are age of the pregnant woman (less than 20 years and more than 35 years); the presence of extragenital pathology (thyroid diseases and the presence of hypertension); combination of somatic morbidity with concomitant genital pathology (menstrual disorders, chronic adnexitis); complicated course of pregnancy in the first trimester (threat of abortion, anemia); disorders of the fetoplacental complex (according to ultrasound observation in the first trimester of gestation and at the beginning of the second trimester).

Among the large volume of laboratory indicators, in the first trimester the most informative were concentration of PL (placental lactogen), hCG (human chorionic gonadotropin), CRP (cortisol) and E_3 (estriol); immunoregulatory coefficient, CD56+ content, level of total hemolytic activity of complement, presence of AFA; indicators of APTT, ART, FFDP, TPI and PgI_2 /TxA_2. At the beginning of the second trimester, in addition to this, informative were ultrasound monitoring data of FPC, changes in the concentration of Pg (progesterone), PL, E_3 and Kr.

In the comparative analysis of the ratio of singularity, prognostic coefficient and information value, the highest values of the above parameters were established, which formed the basis of the prognostic model for assessing the degree of individual risk of maladaptive disorders in the fetoplacental complex in women with GOS (only 34 of the 46 indicators remained). The basic principles of our proposed methodology are presented in Table 2.

At the same time, we used the most convenient

Table 2

Methods of prediction of maladaptive disorders in the fetoplacental complex

Name of the features	Predictive coefficient (points)
Age:	
- up to 20 years	3,0
- more than 35 years	3,0
Extragenital pathology:	
- thyroid gland diseases	6,0
- arterial hypertension	4,5
Gynecological pathology:	
- inflammatory processes of the genitalia	3,5
- menstrual irregularities	3,5
Complications of this pregnancy in the first trimester:	
- threat of interruption	4,0
- anaemia	5,0
Ultrasound I trimester:	
- chorion hypoplasia	3,0
- thickening «decidua basalis»	3,5
Second trimester ultrasound:	
- placental hypertrophy	3,0
- placental hypoplasia	4,0
- hypertension of the myometrium	3,5
- polyhydramnios	3,0
- oligohydramnios	4,0
- destructive changes in the placenta	3,0
- FGR	6,0
Endocrine status I trimester:	
- PL< 30%	3,5
-HCG< 30%	4,0
- E_3 <30%	3,0
-Cr >30%	4,0
II trimester:	
-P <40%	3,5
- PL <40%	4,0
-Cr >40%	5,0
- E_3 <40%	4,5
Immune status I trimester:	
- CD4+/CD8+ >2	5,0
- CD56+ >25%	5,0
- SN50 >30%	4,5
AFA:	
- available	4,0
The state of hemostasis I trimester:	
- APTT< 30 sec	3,5
- ART >70 sec.	4,0
- TPI >20 c.u.	4,0
- FFDP>2x10 g/l	3,0
- PgI_2 /TxA_2 <0.8	4,0

point system for practical health care. Assessment of the degree of individual risk is more appropriate in the first trimester and early second trimester of the gestational period. This approach, in our opinion, is the most rational in terms of effective treatment and preventive measures. For its practical application, three degrees of individual risk of maladaptation disorders in the fetoplacental complex are proposed: high, medium and low.

In the first trimester: – high – more than 40 points; – average – from 31 to 40 points; – low – up to 30 points. At the beginning of the second trimester: – high – more than 50 points; – average – from 41 to 50 points; – low – up to 40 points.

It is now established that in the process of placentation a unique vascular remodeling occurs. In the process of deep invasion of cytotrophoblast cells during the formation of the placenta, almost complete transformation of the decidual and myometrial segments of the spiral arteries occurs. Defective placentation was originally described in connection with preeclampsia and fetal growth retardation (FGR), but now there is evidence that it is also associated with other great obstetrical syndromes, including spontaneous abortion, preterm birth and premature rupture of membranes [8–12]. It has been repeatedly emphasized that great obstetric syndromes have common pathological mechanisms.

The main of them are vascular pathology, hemostasis disorders, immune response pathology (inflammation), endocrine disorders and instability to adverse environmental toxic factors [13–15]. Normally, in physiological pregnancy, the cytotrophoblast migrates from the chorionic villi and penetrates into the uterus, reaching the inner layer of the myometrium. The cells of the placenta, in this case, half contain maternal genes, and half – paternal, that is, for the mother's body they are semi-homologous.

In the uterine wall, the cytotrophoblast penetrates into the spiral arteries and reaches their endothelial lining, while lysis of the smooth muscle wall occurs, due to which the spiral arteries acquire the properties necessary for adequate perfusion of the placenta. In great obstetric syndromes, there is a violation of the depth of penetration of cytotrophoblast cells, gestational transformation of the spiral arteries is not fully carried out, which is associated with impaired remodeling and obstructive lesions [6, 22, 23].

The identified features of obstetric and perinatal pathology in pregnant women who had complications from the GOS group can serve as markers for predicting the risk of a significant increase in obstetric and perinatal complications in the mother and fetus in these pregnant women. In our opinion, further analysis of functional, instrumental and laboratory parameters in women of the prognosis group allowed us to identify the most informative prognostic criteria for the development of GOS, and allowed us to develop a more effective methodology for predicting obstetric and perinatal complications in these women.

CONCLUSIONS

Multidimensional analysis of anamnestic data, features of pregnancy, basic clinical, laboratory and functional parameters in women with clinical manifestations of GOS, allowed us to develop an effective method of predicting the risk of GOS. This method can be really used in obstetric hospital of any level, and on its basis – to take specific treatment and preventive measures at all stages of management of women of this group.

Clinical testing of the scoring method of prediction showed its high sensitivity (91.8%) and specificity (85.6%). After verification of the quantitative assessment system, the research results have been implemented in clinical practice, which will be described in more detail in the next publication.

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ГІНЕКОЛОГІЯ

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