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Keywords: Pregnancy-induced hypertension, obstetric ultrasound, doppler velocimetry, fetal biophysical score, risk coefficient for complications

**INTRODUCTION**

HTAIS / PE is the main cause of perinatal morbidity and mortality, affecting both the fetus and the mother, which led me to research in my doctoral thesis, the main clinical-paraclinical aspects of HTAIS to establish a practical model for calculating a coefficient risk of complications with predictive value.

**CURRENT STATE OF KNOWLEDGE**

**1. PREGNANCY-INDUCED BLOOD PRESSURE**

Gestational hypertension - pregnant women whose blood pressure reaches and exceeds 140 / 90mm Hg for the first time in the second half of pregnancy but who do not have proteinuria.

Preeclampsia (PE) - diastolic BP greater than or equal to 110mm Hg, systolic BP greater than or equal to 160mm Hg, proteinuria absent or positive, headache present, visual disturbances present, upper abdominal pain present, oliguria present, convulsions (eclampsia) present, elevated serum transaminases, thrombocytopenia below 100,000 / mmc, obvious intrauterine growth restriction, pulmonary edema present.

PE superimposed over chronic hypertension - PE superimposed over chronic hypertension is a clinical form of hypertension in pregnancy in patients with a history of chronic hypertension, which occurs during pregnancy proteinuria over 0.3 g / L / 24 hours and exacerbation of pre-existing BP.

Eclampsia (E) - initially, a prodromal condition manifested by headache in 40% of cases, sudden increase in BP, visual disturbances, vertigo, epigastric pain in the bar, followed by a convulsive crisis that includes 3 stages: period of invasion, period tonic seizures, period of clonic seizures, coma.

HELLP-It is a complication of HTAIS clinically characterized by severe pain in the upper abdominal floor, caused by hyperdistension of the liver capsule, a consequence of the
appearance of an intrahepatic hematoma, which by overpressure can rupture with the appearance of severe hemoperitoneum.

2. Uteroplacental apoplexy (AUP) is usually accompanied by placental abruption, intrauterine death of the fetus, necrosis of the uterus, fluid-coagulant disorders.

2. HTAIS ETHIOPATOGENICITY

Normally, the trophoblast invades the spiral arteriole in 2/3 (middle and terminal). In cases of PE the invasion is incomplete, only in 1/3 terminal. The middle portion remains intact, ie sensitive to vasopressor stimuli. Prolonged vasospasm alters the endothelium of the spiral arteries. Platelets repair the lesions. The phenomenon of endotheliosis or acute atherosis occurs. The vasorum vessel reactive to vasopressors maintains vasoconstriction. Platelets agglutinate and release thromboxane A2, a potent vasoconstrictor. Increased ischemia is self-sustaining by destroying the secretory endothelium, and discharges of vasodilators (PGE2, PGI2, angiotensinase, bradykinin, nitric oxide are eliminated - calcium secreted by calmodulin is released, contraction).

Increases the vasorum vessel pressor response to angiotensin II and thromboxane A2, endothelin, and calcium. Decreases the release of plasminogen activator, increases the release of Willebrandt factor, increases the circulation of ET-1, fibronectin.

There can be noticed deposits of fibrin, hyaline tissue, vessels rupture due to ischemia and vascular wall necrosis, hemorrhages, thrombosis, local chorio-deciduous infarcts, in the uterus and various other organs, as seen in severe PE, eclampsia, utero-placental apoplexy, HELLP syndrome, large vulvo-vaginal hematoma.

3. FETAL ANNEXES

(TRANSITIONAL BIOLOGICAL GESTATIONAL SYSTEM)

SBTG according to the authors is a transient biological system of connection, nutrition and feto-maternal protection corresponding to fetal appendages (placenta, SBTG according to the authors is a transient biological system of connection, nutrition and feto-maternal protection corresponding to fetal appendages (placenta, amniotic membranes, umbilical cord, amniotic fluid amniotic membranes, umbilical cord, amniotic fluid)
4. BIOPHYSICAL EXPLORATIONS IN PREECLAMPSY
Fetal electrocardiographic monitoring
Conventional transabdominal ultrasound
Manning fetal biophysical score (SBF)
Doppler velocimetry

PERSONAL CONTRIBUTION

5. WORKING HYPOTHESIS
The accurate assessment of the risks of preeclampsia, eclampsia, utero-placental apoplexy, HELLP syndrome, against the background of induced hypertension or pre-existing pregnancy, is extremely important to improve the vital and functional maternal-fetal prognosis. It is known that this pathology associated with pregnancy increases the risk of maternal and neonatal mortality and morbidity.

6. GENERAL OBJECTIVES
Ultrasonographic study in patients with HTAIS / PE associated with the prediction of maternal accidents and complications (severe preeclampsia, eclampsia, utero-placental apoplexy, intrahepatic hematoma, cerebral haemorrhage, acute pulmonary edema, large vulvo-vaginal hematoma) and intrauterine complication, fetal death in utero) will be analyzed in this doctoral thesis.

7. MATERIAL AND METHOD
This research study was conducted both retrospectively and prospectively, taking place between 2014 and 2018, on a study group consisting of 324 selected patients diagnosed with HTAIS / PE. Pregnant women with incomplete clinical and ultrasound examinations, pregnant women with epilepsy and those who could not be fully monitored due to their addressability to other doctors or other hospitals were excluded from the study, resulting in 268 patients included in the study.

The cases included in the study were selected from the case study of the obstetrics-gynecology department of the Drăgășani City Hospital and the private practice of the personal obstetrics-gynecology practice, as well as from the private practice of two other obstetrics-gynecology practices in Dolj County.

The 268 pregnant women with HTAIS / PE included in the study were analyzed on the following parameters: age, place of origin, marital status, level of education, personal pathological history, body mass index, obstetric history.

We collected clinical information noting the following aspects: obstetrical consultation, hematological investigations, urinary investigations, Gant / Roll over test, cardiological consultation and electrocardiogram, nephrological consultation, neurological consultation, ophthalmological consultation, anesthesia-intensive care consultation, fetal cardiotocography / Non-Stress -Test.

We collected ultrasonographic information noting the following aspects: complete ultrasound study of the fetus and fetal appendages, fetal biophysical profile Manning, doppler velocimetry
in the uterine, umbilical, middle cerebral artery and cerebro-placental ratio, following the pulsatility index (IP) and resistance index (IR), the presence or absence of the protodiastolic incision in the uterine artery, the presence, absence or reversal of end-diastolic flow on the umbilical artery

8. RESULTS

By applying the exclusion criteria, a group of 268 pregnant women included in the final study was obtained, a group consisting of 97 patients with severe PE and 171 patients with non-severe PE. The control group consisted of 124 pregnant women without PE, in whom the pregnancy went without complications.

The mean age in the patients in the study group with non-severe PE was 28.15 (± 46.28) years, in those with severe PE 33.65 (± 36.13) years, while in the pregnant women in the control group, the age mean was 24.5 (± 14.9) years, indicating the increased significance of the age parameter in the occurrence of PE (t = -6.62, p <0.05).

Regarding: the environment of origin of the patients, the marital status, the level of training, the parity, we found a statistically insignificant result.

Statistical analysis showed a significant correlation of personal pathological history with the presence of severe PE in patients in the study group (χ² = 50.84, p <0.05).

From the point of view of BP, the patients in the studied group showed an increase in BP 150.04 (± 12.9) mm Hg and BP 95.58 (± 7.5) mm Hg, and the pregnant women in the control group had BP s 112.06 (± 12) mm Hg and BP d 75.73 (± 6.8) mm Hg.

From the point of view of the Body Mass Index (BMI), the patients from the studied group were: 49 normal-weight (18.3%), 162 overweight (60.4%), 57 obese (21.3%), and the pregnant women from the control group were: 68 normal-weight (54.8%), 41 overweight (33.1%) and 15 obese (12.1%).

Statistical analysis shows the correlation of an increased BMI with the presence of preeclampsia in the study group, the most numerous being overweight patients (p <0.05).

Ultrasound-estimated fetal weight was monitored in pregnant women in the two groups to highlight intrauterine growth restriction (IUGR) versus normal development. In the patients in the control group, we found 117 normal-weight fetuses (94.4%) and 7 fetuses with intrauterine growth restriction (5.6%). In the patients from the studied group, we found: 43 normal-weight fetuses (16.04%), 54 fetuses with IUGR (20.15%) in severe PE pregnant women and 95 normoponderal fetuses (35.45%), 76 fetuses with IUGR (28 , 36%) in pregnant women with non-severe PE.

The statistical analysis performed between the 2 groups of the studied group, in terms of estimated fetal weight is insignificant (χ² = 3.12, p = 0.07, p > 0.05), but between the studied group and the control group denotes the correlation RCIU with severe and non-severe PE (χ² = 68.50, p <0.05).

The fetal biophysical profile was evaluated to assess fetal well-being during pregnancy. SBF 10 was in 12 patients with severe PE (4.48%) and in 36 pregnant women with non-severe PE (13.43%). We found SBF 10 in 48 pregnant women (17.91%) in the study group, compared to 82 patients (66.13%) in the control group. SBF 8 was in 48 pregnant women with severe PE
(17.91%) and 86 pregnant women with non-severe PE (32.09%), so in the studied group there were 134 patients (50%), compared to 26 pregnant women in the control group (20.97%). SBF 6 was in 25 pregnant women with severe PE (9.33%) and 30 pregnant women with non-severe PE (11.20%), so in the study group there were 55 patients (20.53%), compared to 16 pregnant women in control group (12.90%). SBF less than 6 was in 12 pregnant women with severe PE (4.48%) and 19 pregnant women with non-severe PE (7.08%), so in the study group there were 31 patients (11.56%), and no was recorded in no pregnant woman in the control group.

The statistical analysis between the studied group and the control group denotes the correlation of SBF with severe and non-severe PE ($\chi^2 = 96.27$, $p <0.05$), but the analysis between the 2 groups of the studied group is not significant ($\chi^2 = 4.73$, $p = 0.19$, $p> 0.05$).

We studied Doppler velocimetry in the uterine artery (AU), on the three parameters: IP, IR, S / D, in patients from the two groups. The IP in the studied group had higher values ($1.78 \pm 0.17$ in patients with severe PE and $1.47 \pm 0.06$ in pregnant women with non-severe PE) compared to the control group ($0.88 \pm 0.11$), significantly increased values (t-Student, $p <0.05$).

IR had values of $0.75 \pm 0.03$ in patients with severe PE and $0.66 \pm 0.03$ in pregnant women with non-severe PE in the study group and values of $0.50 \pm 0.03$ in the control group, significantly increased values (t-Student, $p <0.05$). S / D was higher in the study group ($2.78 \pm 0.13$ in patients with severe PE and $2.39 \pm 0.04$ in pregnant women with non-severe PE) compared to the control group ($2.38 \pm 0.78$), significantly increased values (t-Student, $p <0.05$).

We determined the Doppler velocimetry in the umbilical artery (AO) in the patients from the two groups, through the three parameters: IP, IR, S / D. The IP in the studied group had higher values ($1.59 \pm 0.02$ in patients with severe PE and $1.17 \pm 0.02$ in pregnant women with non-severe PE) compared to the control group ($0.92 \pm 0.05$), Significantly increased IP ($p <0.05$). IR had values of $0.79 \pm 0.03$ in patients with severe PE and $0.72 \pm 0.02$ in pregnant women with non-severe PE in the studied group and values of $0.61 \pm 0.06$ in the control group, significantly increased IR ($p <0.05$). The S / D ratio was higher in the studied group ($4.56 \pm 0.45$ in patients with severe PE and $3.42 \pm 0.04$ in pregnant women with non-severe PE) compared to the control group ($2.76 \pm 0.02$), significantly increased S / D ($p <0.05$).

We determined Doppler velocimetry in the middle cerebral artery (ACM) in patients in the two groups. The IP in the study group had lower values ($1.63 \pm 0.02$ in patients with severe PE and $1.66 \pm 0.03$ in pregnant women with non-severe PE) compared to the control group ($1.78 \pm 0.09$).

IR had values of $0.77 \pm 0.06$ in patients with severe PE and $0.80 \pm 0.08$ in pregnant women with non-severe PE in the study group and values of $1.61 \pm 0.05$ in the control group. The S / D ratio was lower in the studied group ($4.11 \pm 0.42$ in patients with severe PE and $2.72 \pm 0.13$ in pregnant women with non-severe PE) compared to the control group ($4.96 \pm 0.69$).

The values of the indices are lower, both in the studied group compared to the control group and in the severe PE group compared to the non-severe PE group.

The cerebro-placental ratio (CPR) of the pulsatility index between the middle cerebral artery and the umbilical artery showed values of $1.03 \pm 0.15$ in patients with severe PE and $1.41 \pm 0.03$ in pregnant women with non-severe PE and values of $1.94 \pm 0.16$ in the control group, significantly low CPR ($p <0.05$).
From the point of view of fetal weight at birth, in patients in the control group, we found: 7 faces weighing between 2001-2500 grams (5.65%), 33 faces weighing between 2501-3000 grams (26.61%), 57 faces weighing between 3001-3500 grams (45.97%) and 27 faces weighing between 3501-4000 grams (21.77%).

In the studied group, in terms of fetal birth weight, we obtained the following results: 17 cases weighing between 1500-2000 grams (6.34%), 61 cases weighing between 2001-2500 grams (22.76%), 147 cases weighing between 2501-3000 grams (54.85%), 43 cases weighing between 3001-3500 grams (16.05%).

Fetal weight was correlated with the intrauterine growth restriction present in PE due to vasospasm, its consequence being fetal hypoxia and nutrient transport deficit through the placental villous system ($\chi^2 = 118.62, \ p < 0.05$).

The Apgar score at birth, in the control group, was: AI 9-10 in 98 cases (79.03%), AI 7-8 in 24 cases (19.36%), AI 5-6 in 2 cases (1.61%). In the studied group, we noticed AI 9-10 in 16 cases (5.97%), AI 7-8 in 172 cases (64.18%), AI 5-6 in 65 cases (24.25%), AI 1-4 in 6 cases (2.24%) and 9 cases of intrauterine stillbirth (3.36%).

Apgar score at birth directly reflects the influence of PE on the intrauterine condition of the fetus ($\chi^2 = 216.95, \ p < 0.05$).

In the study group, we found that the evolution was as follows: 97 pregnant women had severe PE, 171 patients had non-severe PE. Of the 97 severe PEs, 19 cases progressed with serious complications: 7 cases of eclampsia, 5 cases of utero-placental apoplexy, 3 cases of HELLP syndrome, 4 cases of bulky vulvo-vaginal hematoma at birth.

In our research we tried to establish whether it is possible to calculate a risk factor for complications (CRC) in cases with HTAIS.

The parameters taken into account for each patient were marked with 1 point:

1. TA higher than 140/90 mm Hg – 1 point
2. A personal pathological antecedent present - 1 point
3. IMC over 35 kg/m² - 1 point
4. Protein-uria higher than 0.3 g/l/24 hour-1 point
5. Higher uricemia than 6.5 mg% - 1 point
6. NST areactiv – 1 punct
7. SBF smaller or equal than 6 -1 point
8. Index of pulsatility in uterine artery increased – 1 point
9. Index of pulsatility in umbilical artery increased – 1 point
10. Index of pulsatility in cerebrall median artery decreased – 1 point
11. The calculation formula is: CRC = (patient's age × score obtained) / 100

As noted, CRC increases in direct proportion to the patient's age and the number of associated parameters. The minimum value is recorded at 15 years and an associated parameter CRC = 0.15. The maximum value is recorded at 45 years and ten associated parameters CRC = 4.5.

The risk of complications (eclampsia, utero-placental apoplexy, HELLP syndrome, large vulvo-vaginal hematoma, cerebral hemorrhage, acute pulmonary edema) is all the higher as the value of the risk coefficient approaches 4.5.
This formula is useful for the practitioner in order to hospitalize the patient in time, for permanent monitoring and to establish a therapeutic, medical, obstetric or surgical decision.

9. DISCUSSIONS

It is known that gestational hypertension complicates 5-10% of pregnancies, this pathology being an important public health problem worldwide. Age is an important parameter in the occurrence of HTAIS, noting in practice the increase in the incidence of complications progressively with the advancing age of patients. After the age of 35, we noticed the appearance of retroplacental hematoma with a high risk of fetal death. Personal pathological history - renal diseases through the secretion of vasoconstrictor substances and increased resistance in the renal arteriolar flow, proteinuria and increased sodium reabsorption, endotheliosis of glomerular vessels with impact on filtration function and consequently increased serum creatinine and nephropathy, diabetes mellitus by angiopathy Diabetic, pre-existing hypertension in pregnancy due to vascular damage, are risk factors for the occurrence of hypertension / PE.

Obesity is another risk factor associated with preeclampsia; the relationship between obesity and preeclampsia is progressive during pregnancy. This corresponds to an increase from 4.3% in cases with a BMI below 20 Kg / m2, to 13.3% when the BMI is over 35 Kg / m2. IUGR for gestational age estimated by ultrasound, present in severe forms of preeclampsia is due to severe and persistent vasospasm in the uterine artery with a significant reduction in the supply of oxygen and nutrients to the placental intervillous space.

At the same time, the reduction of amniotic fluid to severe oligoamnios below 200 ml, corresponding to an AFI less than 5 cm, an SBF below 4 repeated at 6 hours interval, the presence of the inverted diastolic end in the umbilical artery flow is installed. The presence of these parameters indicates the restriction of intrauterine growth, simultaneously with the onset of fetal distress and the presence of a high risk of fetal death in utero.

PBF evaluates and monitors the fetal intrauterine condition, detects fetal hypoxia in a timely manner, so that the fetus is extracted from the harmful intrauterine environment, without permanent sequelae.

Doppler velocimetry in the uterine, umbilical, middle cerebral artery, along with fetal biometrics, the amount of amniotic fluid and the appearance of the placenta are biophysical, ultrasonographic parameters, which together with clinical parameters indicate suggestive relationships about the fetal intrauterine condition. The pulsatility index and the resistance index highlight the increased resistance in the maternal-fetal circulation and indicate hypoxia and fetal acidosis. The absence or reversal of diastolic flow on the umbilical artery is directly proportional to the degree of fetal hypoxia. This confirms the presence of vasospasm, increasing the resistance of the vascular wall to blood flow. Consequently, the intake of oxygen, nutrients and electrolytes in the intervill area is reduced, which causes chronic fetal distress.

Doppler velocimetry in the middle cerebral artery revealed low values compared to the control group, due to the phenomenon of preservation of cerebral circulation. The phenomenon of centralization of the circulation is the one that protects the fetal brain, the pulsatility and
resistance indices being slightly increased, almost negligible, in cases of severe PE, precisely to counteract the possible pathological effects of hypoxia and metabolic acidosis on fetal brain structures. This aspect is also explained by the fact that the ratio between the pulsatility index in DHW and IP in AO must always be superunitary. When the ratio is below one, the intrauterine condition of the fetus is very serious, it is imminent death in utero.

Fetal weight at birth in the study group was in about one third of cases corresponding to the intrauterine growth restriction, somewhat in line with the estimated fetal weight ultrasound in the last weeks of gestation. This finding was accompanied by similar changes in doppler velocimetry indices in the middle uterine, umbilical, and cerebral artery. The pulsatility index was increased in cases of severe PE compared to cases of non-severe PE. Patients with severe PE had both changes in fetal biophysical score parameters and doppler velocimetry in the uterine, umbilical and middle cerebral arteries, especially in cases where restriction of intrauterine growth was associated with high blood pressure.

In the study group, approximately half of the fetuses received an Apgar score of 7-8 and a quarter of the cases had Apgar 5-6, which indicates a degree of chronic fetal distress in cases with severe PE. The cases of severe PE had a much more serious evolution compared to non-severe PE.

To predict possible maternal-fetal complications in cases of PE, we proposed a practical and quick formula for calculating the risk coefficient for the occurrence of these complications (CRC). The formula takes into account the patient's age and the main associated parameters, numbered with a dot, being useful for any practitioner, in any profile unit.

The risk coefficient for complications (CRC) increases from 0.15 to 15 years, to 4.5 to 45 years and is directly proportional to the patient's age and the number of associated parameters. CRC has a signal value for the occurrence of a major complication of HTAIS, such as: severe preeclampsia, eclampsia, utero-placental apoplexy, HELLP syndrome, large vulvovaginal hematoma.

The originality of the paper consists in the fact that I propose the practical and fast calculation of this risk coefficient for the possible evolution towards the complications of HTAIS. This formula is useful for the practitioner in order to hospitalize the patient in time, for permanent monitoring and establishing a therapeutic, medical, obstetric or surgical decision, in order to trigger and direct the birth by natural means, fetal extraction by forceps when the conditions are met. obstetric, extraction by cesarean section.

By calculating the CRC retroactively to the studied cases, we found the veracity of the formula, the value of the coefficient being towards the maximum limit in cases complicated with eclampsia, HELLP syndrome, retroplacental hematoma, severe form / uteroplacental apoplexy. The objective of the study on the prediction of complications in patients with HTAIS was achieved by systematic monitoring by ultrasound and arterial Doppler study, along with the associated parameters taken in the calculation of the risk coefficient for complications.
10. CONCLUSIONS

Early identification of worsening HTAIS involves the prevention of maternal complications (eclampsia, HELLP syndrome, utero-placental apoplexy) and fetal complications (IUGR, prematurity, fetal death in utero).
Prediction of complications in patients with HTAIS was made by systematic monitoring by ultrasound and arterial doppler study, along with associated parameters taken in the calculation of the risk coefficient for complications.
The risk coefficient for complications (CRC) in HTAIS is directly proportional to the patient's age and associated parameters and can vary between 0.15 - 4.5.
Analysis of clinical data showed that age, body mass index before pregnancy, the presence of pre-existing chronic hypertension in pregnancy with the addition of hypertension, the presence of personal pathological history, were significantly correlated with the risk of complications in the last trimester of pregnancy and birth.
Early clinical-paraclinical and especially ultrasound monitoring ensures an adequate completion of the term pregnancy and birth.
Analysis of ultrasound data showed that the existence of IUGR at current pregnancy, the value of fetal biophysical score and Doppler velocimetry in the uterine, umbilical and middle cerebral artery, cerebro-placental ratio, were significantly correlated with the risk of complications in the last trimester of pregnancy and during birth.
The pulsatility index and resistance index were increased in severe PE for the three arteries explored. The coexistence of the protodiastolic incision, the notch-ing in the uterine artery, the inverted end in the umbilical artery, the value below 1 of the cerebro-placental ratio denotes acute fetal distress, with an imminent risk of fetal death in utero by hypoxemic hypoxia and metabolic acidosis.
Fetal ultrasound, fetal biophysical score and multivascular Doppler velocimetry are of major importance in establishing obstetric attitude, vaginal birth or fetal extraction by cesarean section, in correlation with fetal intrauterine vitality and estimated fetal weight prenatally.
Monitoring the maternal-fetal evolution in HTAIS, from a clinical, biochemical, ultrasound point of view and through interdisciplinary consultations is extremely important for obstetric practice.
The monitoring of the maternal-fetal evolution and the early identification of the worsening of PE determines the improvement of the vital and functional maternal-fetal prognosis in HTAIS. The most complete recovery of the mother's health allows an optimal life with a good prognosis, reproductive and maternal, in the future. Cases with chronic hypertension, pre-existing pregnancy, over which HTAIS overlaps are of particular interest to parturients after the age of 35 and are more frequently accompanied by postpartum complications, maintaining hypertension.
Biophysical examinations in the monitoring of cases of HTAIS determine the reduction of perinatal morbidity and improve the feto-maternal prognosis.