КЛІНІЧНІ ДОСЛІДЖЕННЯ

SPECIALTIES OF COURSE OF EARLY AND LATE PREECLAMPSIA IN WOMEN IN VINNITSYA REGION

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Annotation. *Preeclampsia is one of the leading causes of maternal and perinatal death, and it complicates from 5 to 8% of all pregnancies. The aim of the research was to show the differences in anamnesis, diagnostics and prognosis, in groups of pregnant with hypertensive disorders. Retrospective investigation included 138 delivery histories and perinatal record cards from Vinnitsya Municipal Clinical Maternity hospital №1, in a period from 2016 till 2018. Women were divided into two investigated groups: I - 36 women with early preeclampsia, and II group - 52 women with late preeclampsia, and a control group of 50 women. The structure of somatic and gynecological diseases of pregnant women was studied, the severity of preeclampsia and the condition of the newborn were assessed according to the Apgar scale. Statistical processing of the obtained results was performed by odds ratio, its standard error and 95% confidence interval were calculated according to D. G. Altman (1991). It is established that in women with obesity or excessive body weight (every second women in groups), and those who had cardiovascular disorders (twice more often with late preeclampsia) developed preeclampsia more often, comparing to control group. All cases of antenatal and early neonatal death of newborn were registered in a group with early preeclampsia, which points out on heavier flow of the disease and different pathogenesis. Cases of early pregnancy toxemia and edema of pregnant occurred twice more often, in group with early preeclampsia, and ran more heavy (up to the development of ascites), comparing to the second group. Debut of symptoms was earlier, that requires earlier prophylaxis (since week 12). Fetal intrauterine growth retardation, reversible and high resistant blood stream during ultrasound were marked only in group with EP. In future, this research together with pathohistological investigation of placentas and immunohistochemical research of those tissues, can underlie predictive and preventive personalized system for early and late preeclampsia.*

Keywords: *early and late preeclampsia, pregnancy toxemia, placental status.*

Introduction

Preeclampsia is one of the leading causes of maternal death - 60 000 annually, and it complicates from 5 to 8% of all pregnancies. It has been proven; in clinical and experimental researches, that gestational endotheliopathy is a basic mechanism in the development of hypertensive disorders during pregnancy [1, 3, 10, 11]. The problem is particularly important in developing countries in where the incidence of hypertensive disorders of pregnancy is higher and maternal mortality rates are 20 times higher than those reported in developed countries. Risk factors for the development of PE include obesity, insulin resistance and hyperlipidemia that stimulate inflammatory cytokine release and oxidative stress leading to endothelial dysfunction (ED) [9]. Gestational endotheliopathy results into ischemia, hypoxia and oxidative stress, and plays the leading role in development of preeclampsia. Clinical tests and experimental research have suggested that generalized endotheliosis in the systemic, renal, cerebral, and hepatic circulation could decrease endothelium-derived vasodilators such as nitric oxide, prostacyclin, and hyperpolarization factor and increase vasoconstrictors such as endothelin-1 and thromboxane A2, leading to increased vasoconstriction, hypertension, and other manifestation of preeclampsia [8]. Preeclampsia that develops in terms less than 34 weeks is called early preeclampsia, after 34 weeks - late preeclampsia. Origin of early preeclampsia is related to inadequate invasion of trophoblast, hypoxia in placenta and release of biologically-active substances, that in future will influence endothelia [6]; in case of late preeclampsia it`s mostly connected with maternal cardiovascular system, that will influence integration of endothelia [1]. Early preeclampsia folds 5-20% and clinically flows more difficult. Late preeclampsia presents 80% and is extremely rare accompanied by fetal growth retardation and violation of blood stream in uterine vessels. PE survivors will have at twice the risk of heart disease and stroke, and four times the risk of high blood pressure in the future [4].

The aim of the research was to show the differences in anamnesis and their statistical significance in diagnostics and prognosis, in groups of pregnant with hypertensive disorders.

Materials and methods

During the research there was conducted a retrospective and statistical analysis of 138 delivery histories and perinatal record cards from Vinnitsya Municipal Clinical Maternity hospital №1, in a period from 2016 till 2018. Women were divided into two investigated groups: I - 36 women with early preeclampsia, and II group - 52 women with late preeclampsia. Control group - 50 women with uncomplicated pregnancy and delivery. Main diagnostically significant indexes were determined, which later underwent comparative analysis for all groups. The structure of somatic and gynecological diseases of

pregnant women was studied, the severity of preeclampsia and the condition of the newborn were assessed according to the Apgar scale. Statistical processing of the obtained results was performed by odds ratio, its standard error and 95% confidence interval were calculated according to D. G. Altman (1991).

This work was carried out within the R & D "Optimization of early diagnostics and preventive treatment of perinatal complications caused by gestational endotheliopathy" № state registration 0121U109141.

Results. Discussion

All pregnant were living in equal terms (Vinnitsya, Ukraine) and mainly engaged in mental work, no occupational hazards were marked. Only tobacco smoking was marked in 1.9% (till week 20) in II group, and 2% - in control group. Age of pregnant varied between 17 and 42 years. Middle age of women was 26-30 years; which made 38.9% in I group, 28.8% - in II group and 36% in control group. Average gestational terms in groups were 36-41 weeks. Coming out from our data only 1 woman in I group and 1 in II, had preeclampsia in previous pregnancies; none of women marks family history of preeclampsia.

According to our data in childhood, all women had various infectious diseases, which were: chicken pox, measles, epidemic parotitis, scarlet fever, hepatitis A, rubella, tonsillitis and pneumonia. However, frequency of such cases in investigated groups did not have significant difference from average in population.

Because of the role of the vascular factor in the development of PE, the analysis of episodes of cardiovascular disorders (vascular dystonia, arterial hypertension, various violations of cardiac rhythm and mitral valve prolapse) and other extra genital pathologies was conducted in groups. Such as diseases of urogenital system, that included chronic pyelonephritis, urolithiasis, chronic cystitis; also varicosity, goiter, thyroiditis, rheumatoid arthritis, adenoid disease, diseases of digestive tract and allergies, including allergic reactions to drugs. More detailed comparative analysis is driven in table 1.

Practically every second woman in investigated groups had violation of metabolism of lipids: in the I group - obesity in 15 (41.7%), and also 2 (5.6%) excessive body weight; in II group it is 24 (46.2%) and 3 (5.8%).

Achieved results are similar to D.A. Boris (2020) work results, in which data confirms the influence of such factors: age >36 years, preeclampsia or cardiovascular diseases in anamnesis, violations of lipometabolism that increases risk of the development of preeclampsia [2].

Except somatic diseases percentage of carried out operative interventions was analyzed. Majority was presented by operations on the organs of abdominal cavity and small pelvis. The structure of operations was: herniotomy, laparoscopic cystectomy, appendectomy, removing of cyst of urethra, laparoscopic tubectomy, thyroidectomy, osteosynthesis of tibia-femoral joint,

Table 1. Structure of somatic diseases.

Name of the disease	I group (n=36)	II group (n=52)	OR (95% CI) P
VD/AH	6(16.7%)	18(34.6%)	0.38(0.13-1.08) 0.068
Violation of cardiac rhythm	2(5.6%)	1(1.9%)	3.00(0.26-34.39) 0.38
MVP	2(5.6%)	6(11.5%)	0.45(0.09-2.37) 0.35
Varicosity	3(8.3%)	3(5.8%)	1.48(0.28-7.81) 0.64
Urogenital diseases	7(9.4%)	23(44.2%)	0.30(0.11-0.82) 0.02
Myopia	3(8.3%)	3(5.8%)	1.48(0.28-7.81) 0.64
Goiter	2(5.6%)	10(19.2%)	0.25(0.05-1.20) 0.08
Adenoid disease	0	3(5.8%)	0.19(0.009-3.87) 0.28
Allergies	7(9.4%)	6(11.5%)	1.85(0.57-6.05) 0.31
Rheumatoid arthritis	1(2.8%)	1(1.9%)	1.46(0.88-24.08) 0.79
Diseases of digestive system	8(22.2%)	9(17.3%)	1.37(0.47-3.96) 0.57
Diseases of pulmonary system	0	2(3.8%)	0.28(0.01-5.94) 0.41
Epilepsy	0	1(1.9%)	0.47(0.02-11.87) 0.65
Vitiligo	0	1(1.9%)	0.47(0.02-11.87) 0.65

Table 2. Structure of gynecological diseases.

Name of pathology	I group (n=36)	II group (n=52)	OR (95% CI) P
PCOS	2(5.6%)	0	7.61(0.35-163.36) 0.19
Erosion of the cervix	4(11.1%)	11(22%)	0.47(0.14-1.60) 0.23
CIN	0	2(4%)	0.28(0.01-5.94) 0.41
Disorder of menstrual cycle	1(2.8%)	1(2%)	1.46(0.09-24.08) 0.79
Extrauterine pregnancy	0	3(6%)	0.19(0.009-3.87) 0.28
Infertility	3(8.3%)	0	10.97(0.55-219.19) 0.12
Polyps of the cervical canal	1(2.8%)	0	4.44(0.18-112.03) 0.37
Polyps of endometrium	1(2.8%)	0	4.44(0.18-112.03) 0.37
Myoma	1(2.8%)	2(4%)	0.71(0.06-8,19) 0.79
Ovarian cysts	2(5.6%)	4(8%)	0.71(0.12-4,08) 0.69
Chronic salpingo-oophoritis	0	2(4%)	0.28(0.01-5,94) 0.41

rhinoplasty, hysteroscopy, and operative treatment of Shmorl` nodes. The highest percentage was presented by appendectomy - 11.1% in the I group, 7.7% in the II and 6% in control group; laparoscopic cystectomy was 5.6% in the I group and 1.9% in II group and 0 for control group.

Establishment of menstrual function was also marked. Middle age of the beginning of menstruation for the I group was 12.85±2,5 years, for II group - 13±1.25 years, and for control group - 14±1.4 years.

Structure of gynecological pathologies in investigated groups included PCOS, erosion of the cervix (1.9% (1 case)

Table 3. Division according to the number of deliveries

Number of deliveries	I group (n=36)	II group (n=52)	Control group (n=50)
Primipara	27(75%)	36(69.2%)	24(48%)
Secondparous	5(13.9%)	14(26.9%)	22(44%)
Multiparous	4(11.1%)	2(3.8%)	4(8%)

Table 4. Severity of preeclampsia.

Severity	I group (n=36)	II group (n=52)	OR (95% CI) p
Mild	4(11.1%)	26(50%)	0.13(0.04-0.40) 0.0005
Intermediate	26(72.2%)	22(42.3%)	3,55(1,42-8,84) 0.006
Severe	6(16.7%)	4(7.7%)	2,40(0.63-9,21) 0.20

Table 5. Structure of diseases during pregnancy.

Name of the disease	I group (n=36)	II group (n=52)	OR (95% CI) p
Cold	21(58.3%)	29(55.8%)	1.11(0.47-2.62) 0.81
Pneumonia	0	1(1.9%)	0.47(0.02-11.87) 0.65
Risk of miscarriage	2(5.6%)	3(5.8%)	0.96(0.15-6.06) 0.97
Risk of premature birth	3(8.3%)	2(3.8%)	2.27(0.36-14.35) 0.38
Gestational diabetes mellitus	0	1(1.9%)	0.47(0.02-11,87) 0.65
Anemia of pregnant	9(25%)	17(32.7%)	0.69(0.27-1,78) 0.44
Asymptomatic bacteriuria	0	5(9.6%)	0.12(0.006-2,21) 0.15
Acute sinusitis	0	2(3.8%)	0.28(0.01-5,94) 0.41

in the II group underwent LEEP, and 14% (7 cases) - in control group), CIN (drug therapy), violations of menstrual cycle, ectopic pregnancy (tubectomy done), infertility, polyps of cervical canal, myoma, cysts of the ovaries (I and II group - 1 case of dermoid cysts, II group - 1 case of endometrioid cyst), cysts of vagina, chronic salpingo-oophoritis, and cysts/fibroadenomas of mammary glands (operative treatment was in 1 case (2.8%) in the I group) (tab. 2).

The percent of previous miscarriages on early terms was 5.6% (2) in the I group, 13.5% (7) in the II, and 18% (9) in control group; cases of artificial abortion made 2.8% in the I group, and 14% (7) in control group. Intrauterine fetal death at the term of 38 weeks and weight 1950 grams in previous pregnancy, was marked in the I group, and early neonatal death on fifth day at the term of 27 weeks and weight 890 grams - 2.8%. No episodes of intrauterine or early neonatal death were marked in II or control groups.

The percent of primipara, secondparous and multiparous women is shown in table 3. There is a significant difference in amount of primipara women in I and II groups, comparing to the control group.

In present pregnancy, women from I and II groups were divided into three sub-groups: mild, intermediate and severe preeclampsia (tab. 4).

During pregnancy each women had one of next diseases or conditions: acute respiratory disease, anemia of pregnant, asymptomatic bacteriuria, risk of miscarriage and risk of preterm delivery (more detailed information given in table 5), that statistically did not differ from a control group, and did not confirm its influence on the origin of PE. Unlike our research in dissertation work of F.R. Kutueva (2020) it was statistically proven the influence of the infections of upper respiratory tract, carried on the early terms of pregnancy, and also infections of genital tract, as an increased risk of development of PE: 8.1 and 4.9 times more often; and edema caused by pregnancy - 7.8 times [5].

Also 11.5% (6) of women in II group were carriers of TORCH-infections, only 2% in control group. In the I group early pregnancy toxemia was marked in 8.3% (3 women), edema of pregnant developed in 25% (9), and 2.8% had ascites, 100% had elevated blood pressure before week 34; in II group early toxemia of pregnancy made 1.9% (1), edema - 9.6% (5); in control group all of this indexes made up 0.

Results of ultrasound investigations, on different terms, also were taken into the account. Number of pathological

Table 6. Pathological conditions (according to ultrasound).

Name of the condition	I group (n=36)	II group (n=52)	OR (95% CI) p
Hyperplasia of placenta	9(25%)	10(19.2-%)	1.4(0.50-3.89) 0.52
¯ of feto-placental bloodstream	8(22.2%)	9(17.3%)	1.37(0.47-3.96) 0.57
¯ of utero-placental bloodstream	0	2(3.8%)	0.28(0.01-5.94) 0.41
Cysts of placenta	3(8.3%)	9(17.3%)	0.43(0.11-1.73) 0.24
Hypoplasia of placenta	4(11.1%)	1(1.9%)	6.38(0.68-59.61) 0.10
Olygohydramnion	9(25%)	0	36.27(2.03-646.85) 0.01
Polyhydramnion	2(5.6%)	2(3.8%)	1.47(0.19-10.95) 0.71
UFGR	3(8.3%)	0	10.97(0.55-219.19) 0.12
Low weight fetus	1(2.8%)	2(3.8%)	0.71(0.06-8.19) 0.79
Reverse blood flow	1(2.8%)	0	4.44(0.18-112.03) 0.37
Highly resistive blood flow	1(2.8%)	0	4.44(0.18-112.03) 0.37
Premature aging of placenta	3(8.3%)	0	10.97(0.55-219.19) 0.12
Low placentation	3(8.3%)	0	10.97(0.55-219.19) 0.12

Table 7. Condition of newborn according to Apgar.

Score according to Apgar	I group (n=36)	II group (n=52)
1'-8grade, 5'-9g	27(75%)	44(84.6%)
1'-3g, 5'-7g	0	1(1.9%)
1'-5g, 5'-7g	2(5.6%)	0
1'-6g, 5'-7g	3(8.3%)	0
1'-6g, 5'-8g	2(5.6%)	2(3.8%)
1'-7g, 5'-8g	2(5.6%)	4(7.7%)

conditions of placenta and others were diagnosed: hyperplasia of placenta, decrease of fetoplacental bloodstream, decrease of uteroplacental bloodstream, cysts of placenta, hypoplasia of placenta, polyhydramnion, oligohydramnion, reversible blood stream in umbilical arteries, high resistant blood stream in uterine arteries. Also we found out fetus with low weight according to terms of gestation and intrauterine growth retardation of fetus. This results point out on importance of placental component in development of preeclampsia and consequences for the fetus (tab. 6).

Mode of the delivery was picked individually. For the I group amount of vaginal deliveries was 44.5% (16), those which end up by cesarian section - 55.5% (20), from those urgent CS was in 3 cases; in II group vaginal delivery - 69.2% (36), CS - 30.8% (16), 5 cases of urgent CS among them; which were done because of severe preeclampsia, weakness of childbirth, clinically narrow pelvis and fetal distress. Delivery in control group took place only vaginal way.

During deliveries in the I and II groups such complications took place: dense attachment or defect of particle of placenta, that required hand revision of the cavity of uterus - 3.4% (3) of general amount in both groups, secondary weakness of childbirth took place in 3.4% (3), preterm secretion of amniotic fluid - 2.3% (2), and preterm removing of normally located placenta - 3.4% (3), that needed CS. In control group percent of such complication was less and made only 2% (1 case) - early hypotonic uterine bleeding, that needed hand revision of the uterine cavity and infusion of FFP. Most of the bleedings were marked in I group, that can be possible explained with high system blood pressure, and also in women with hypotonic uterine bleeding or with defect of particle of placenta.

We also estimated the condition of the new-born according to Apgar scale. Almost all new-borns in control group scored on 1 minute 8 grades, 5` - 9 grades, which made 92% (46 new-borns) and 8% (4) who got on 1` - 7 grades, 5` - 8 grades.

Low indexes were marked in new-borns who underwent antenatal distress or had intrauterine fetal growth retardation of I-III degree (tab. 7).

Dissertation work of N.A. Nikitina (2017) "Clinical and imunomorphological features of preeclampsia as a ground of predictive, preventive, personalized system of management of pregnant" established that in diagnostics and in the choice of tactics of management and delivery it's important to point out "early" PE, that more often develops in young first pregnant women and combines with placental insufficiency (almost 68.2%), which is similar to our results, and confirms that early origin of PE can be a predictor of heavy motion of the process and unfavorable maternal and neonatal consequences [7].

Conclusions and perspectives for further developments

1. Women who had obesity or excessive body weight (every second women in groups), and those who had cardiovascular disorders (twice more often with late preeclampsia) developed preeclampsia more often, comparing to control group.

2. All cases of antenatal and early neonatal death of new-borns were registered in a group with early preeclampsia (2.8%), which points on heavier flow of the disease, different pathogenesis.

3. Cases of early pregnancy toxemia and edema of pregnant occurred twice more often in group with early preeclampsia, and ran more heavy (up to the development of ascites), comparing to the second group. Debut of symptoms was earlier, that requires earlier prophylaxis.

4. Fetal intrauterine growth retardation, reversible and high resistant blood stream during ultrasound were marked only in I group.

In future, this research together with pathohistological investigation of placentas and immunohistochemical research of those tissues, can underlie predictive and preventive personalized system for early and late preeclampsia.

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ОСОБЛИВОСТІ ПЕРЕБІГУ РАННЬОЇ ТА ПІЗНЬОЇ ПРЕЕКЛАМПСІЇ У ЖІНОК ВІННИЦЬКОЇ ОБЛАСТІ

Піскун А. О.

Анотація. *Прееклампсія - одна з провідних причин материнської та неонатальної смерті, що ускладнює від 5 до 8% усіх вагітностей. Метою нашого дослідження було показати відмінності в анамнезі, діагностиці та прогнозуванні прееклампсії в групах жінок з гіпертензивними розладами під час вагітності. Ретроспективне дослідження включало в себе 138 історій пологів та обмінних карток на базі Вінницького міського пологового будинку №1, у період з 2016 по 2018 роки. Жінок було розділено на дві досліджувані групи: I - 36 жінок з ранньою прееклампсією та II - 52 жінки з пізньою прееклампсією, а також 50 жінок контрольної групи. Досліджували структуру соматичних і гінекологічних захворювань вагітних, оцінювали ступінь важкості прееклампсії та стан новонародженого за шкалою Апгар. Під час статистичної обробки даних вираховували вірогідність шансів, його стандартну похибку та 95% довірчий інтервал, відповідно до D. G. Altman (1991). Встановлено, що у жінок з ожирінням або надмірною масою тіла (кожна друга жінка в групах), а також у тих, у яких відмічались серцево-судинні захворювання (вдвічі частіше в групі II), частіше в порівнянні з контрольною групою, розвивалась прееклампсія. Усі випадки антенатальної та ранньої неонатальної смерті немовлят були зареєстровані в групі ранньої прееклампсії, що вказує на більш важкий перебіг та дещо відмінний патогенез захворювання. Випадки раннього токсикозу та набряків вагітних вдвічі частіше виникали у групі ранньої прееклампсії та протікали набагато важче (аж до розвитку асциту), ніж у II групі. Дебют симптоматики відбувався раніше, що і потребує більш ранньої профілактики (з 12 тижнів). Затримка внутрішньоутробного розвитку, реверсний та високо-резистивний кровотік під час УЗД відмічався лише в групі I. В майбутньому дане дослідження разом з патогістологічним дослідженням плацент та імуногістохімічним дослідженням може лягти в основу предиктивної та превентивної, персоніфікованої системи діагностики ранньої та пізньої прееклампсії.*

Ключові слова: *рання та пізня прееклампсія, ранній токсикоз, плацентарний статус.*