

ENDOTHELIAL DYSFUNCTION FACTOR AS AN INDICATOR OF CLINICAL AND NEUROLOGICAL DISORDERS IN PREGNANT WOMEN WITH PREECLAMPSIA

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Abstract: we examined 70 pregnant women who were hospitalized in the maternity ward 1-Clinic SamSMI, as well as in the regional perinatal center in the period from 2008 to 2019. The criteria for the inclusion of patients in the study were: in the main group - pregnant women with preeclampsia and in the comparison group - pregnant women with a physiological course of pregnancy in the late period. There is a strong correlation between the manifestations of clinical and neurological changes, as well as laboratory and biochemical parameters (FW, ADMA) and the data of functional diagnostic methods (EEG, Ultrasound investigation of BCV). In turn, these findings help us to identify the risk group in pregnant women with mild preeclampsia for a possible transition to severe preeclampsia, as well as selection of pregnant women among this cohort for possible development of cerebrovascular pathology during pregnancy, childbirth, and the postpartum period. Which makes it possible to select the correct management of pregnancy and childbirth, and thus the treatment, as well as the prevention of cerebrovascular disease in the future.

Keywords: preeclampsia, pregnant women, endothelial dysfunction, von Willebrand factor.

Preeclampsia is one of the most severe complications of pregnancy, childbirth and the postpartum period, making up one of the leading causes of maternal and perinatal morbidity and mortality [1]. In Europe, the frequency of this complication is 2–5%, in developing countries, 12–15% [2, 3, 6, 7, 9, 11, 14].

The pathogenesis of PE has not been fully studied, and the diagnosis and prediction of PE has so far been a difficult task. Today it is considered that hypertensive disorders during pregnancy (including PE) is a complex endothelial dysfunction (endotheliosis), in which there is a violation of growth, differentiation and functioning of the vessels of the placenta, associated with inadequate production of vascular endothelial growth factor, and also violation of the coagulating potential of the blood with the development of the chronic variant of DIC - syndrome [1, 4, 5, 8, 10, 12, 13].

Insufficient understanding of the pathogenesis of preeclampsia significantly limits the development of reliable prognostic examination methods and effective preventive measures. Due to the close connection with the pathophysiology of preeclampsia, dysfunction of the vascular endothelium causes an increased interest of researchers. One of the most studied methods for assessing endothelial function is the determination of specific biochemical markers in the blood, the concentration of which increases with the pathology of pregnancy.

Purpose of the study. To study the clinical neurological and diagnostic parallels in pregnant women with preeclampsia.

Material and methods of research. We examined 70 pregnant women, hospitalized in maternity ward 1-Clinic SamSMI, as well as in the regional perinatal center in the period from 2008 to 2019. Criteria for inclusion of patients in the study were: the core group - pregnant women with preeclampsia and control group - pregnant women with physiological pregnancy at later date.

The main group consisted of 40 pregnant women with a verified diagnosis of preeclampsia in pregnant women aged 17 to 44 years, in gestation from 20 to 42 weeks, which in turn were divided into two subgroups. Of these, 20 women with mild preeclampsia, 20 women with severe preeclampsia.

The comparison group consisted of 30 pregnant women with a physiological course of pregnancy, also from 17 to 44 years, in the period of pregnancy from 36 to 41 weeks. All women underwent a complete clinical and neurological examination, paraclinical examination, including examination of the fundus of the eye, laboratory tests (blood test, urine test, biochemical blood test, prothrombin time, prothrombin index, determination of blood clotting time), as well as from the methods of functional diagnostics of Echo-EG. Methods of functional diagnostics, EEG, Ultrasound investigation of BCV. All women were identified markers of endothelial dysfunction, for example, Willebrand Factor - as an indicator of hemostasis and asymmetric dimethyl arginine (ADMA), as an indicator of the degree of hypoxia.

The results and discussion. Clinical neurological characteristics, laboratory data, and methods of functional diagnostics, including EEG, Ultrasound investigation of BCV, were studied in order to diagnose the severity of preeclampsia, in a correlation aspect. All pregnant women were divided into groups, by age. Of these, pregnant women under the age of 20 years made up 20 women (28.6%), from 21 to 30 years old - 35 women n (50%), from

31 to 40 years old - 13 (18.6%), and over 40 years - 2 (2.6%). If we group pregnant women by the number of comorbidities, it becomes clear that monopathology was observed in 20, which was 28.6%. Two concomitant pathologies were observed in 7 (10%) pregnant women, three pathologies - in 10 (14.3%), four pathologies - in 8 (11.4%), five pathologies - in 5 (7.1%) and also was not about concomitant pathology - in 20 (28.6%) women.

The surveyed pregnant women from the main group presented various complaints, both general and neurological. The most frequent complaints were headaches, which were noted in 30 (75%) pregnant women, edemas, various localization, occurred in 20 (50%). Complaints for increasing of A/P were 18 (45%) women, dizziness in 15 (37.5%), general weakness in 19 (47.5%), nausea and vomiting in 9 (22.5%), pain in the stomach in 16 (40%), irritability in 13 (32.5%), cramping pain and lower abdomen in 8 (20%), the appearance of "flies" before the eyes, noise in the ears, and also congestion in the ear in 7 (17.5%). 5 (12.5%) pregnant women had complaints of double vision in the eyes and eyeshadow, 5 (12.5%) women had numbness in their hands, 7 (17.5%) had poor sleep, 3 (7, 5%) there were complaints from the side of the chest region, also in 4 (10%) pains in the extremities, in 3 (7.5%) there were bouts of convulsions, according to relatives. Pain in the surgical scar was observed in 2 (5%) pregnant women, lack of labor in 2 (5%), tremor in the hands in 2 (5%), tearfulness in 2 (5%), unpleasant sensations in the heart area. 1 (2.5%), lack of air in 1 (2.5%). Among pregnant women, 9 (22.5%) did not make any complaints.

When examining the neurological status in pregnant women from the main group, the following parameters were assessed: cerebral symptoms, CN, motor system, reflex system, coordinating system, sensitive area, vegetative system, and also the higher nervous system. Of the cerebral symptoms, in 2 (5%) pregnant women, cranial pain was observed in the visceral region during percussion, in 1 (2.5%) slight stiffness of the occipital muscles was observed. In the neurological status of the patients, various disorders in the cranial nerve system were noted: decreased vision in 2 (5%) women, restriction of movement of the eyeballs, mostly in the right abduction in 4 (10%), horizontal nystagmus in 29 (72.5%), disturbance of accommodation in 7 (17.5%), disturbance of convergence in 8 (20%), anisokoria in 2 (5%), diplopia in 7 (17.5%), reduction in the reaction of pupils to light in 3 (7.5%) pregnant. In 2 (5%) there was pain in the exit point of the trigeminal nerve and palpation, dizziness in 13 (32.5%), tinnitus in 7 (17, 5%). There was smoothed naso-labial folds for 18 (45%), the deviation of the tongue in 21 (52.5%) of pregnant women. In the motor area: clear paresis, paralysis was not observed in 37 (92.5%) women, hemisyndrome in 3 (7.5%) pregnant women. Changes in the reflex sphere were of the following nature: reflexes of average vitality were observed in 18 (45%), lively reflexes in 16 (40%), increased in 6 (15%). From pathological reflexes, Babinsky pathological reflex was observed in 8 (20%). Research analysis of coordinating system shows that in 15 (37.5%) women staggering occurred in Romberg position, with performance coordinating tests with intension, 11 (27,5%) was noted in position Romberg, observing coordinating tests.

When examining the sensitive area of the patient noted hypesthesia in 3 (7.5). Studying the autonomic nervous system, we can conclude that in these patients dermographism red, diffuse was noted in the majority, accounting for 28 (70%), white, diffuse dermographism in 12 (30%). Distal hyperhidrosis was observed in 15 (37.5%), emotional lability in 12 (30%) pregnant women.

From the methods of functional diagnostics, we used EEG to assess the state of the functional activity of the cerebral cortex. This pregnant women, divided into groups EEG was carried out etc. A comparative analysis of these parameters between the physiological pregnancy and pre-eclampsia (inclusive preeclampsia mild to severe) for a comparative assessment of the functional activity of the cerebral cortex. Based on the EEG values of the above groups in a comparative aspect, it can be concluded that during physiological pregnancy, the normal variant is mainly observed, without pathological deviations, and in the background there is a decrease in the functional activity of the cerebral cortex, and in the last place there is a sharp background rhythm, in small quantities. And in the group of mild pregnant women with preeclampsia, in general, approximately half of these pregnant women experienced a decrease and sharpness of the background rhythm, then paroxysmal activity, and also a quarter of patients had a decrease in the threshold of convulsive readiness of the cerebral cortex. It should be noted that in case of severe pre-eclampsia, the above-mentioned changes were observed, as well as in the case of a slight degree, in addition to which the deformation of the background rhythm and epileptic activity in the form of sharp-spike and sharp-slow waves also joined (fig. 1.).

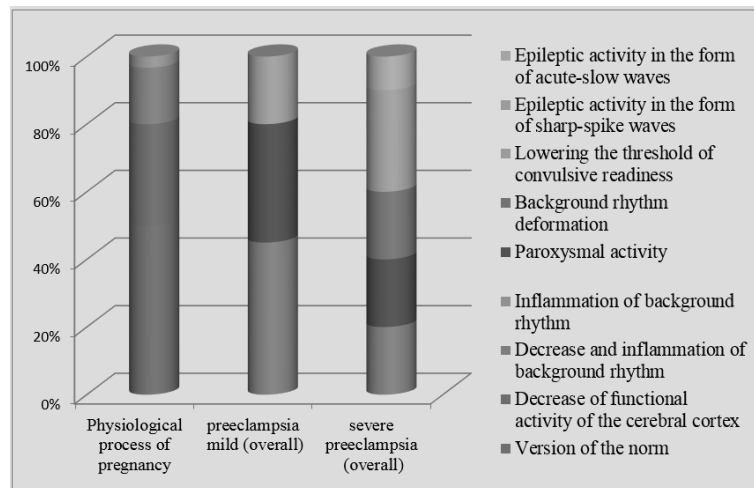


Fig. 1. EEG indicators in a comparative aspect in the physiological course of pregnancy and in preeclampsia of pregnant women

Consequently, which in turn allows us to assume that, the more pronounced the degree of pre-eclampsia, the more varied the EEG changes, and also the convulsive and epileptic activity increases. The next stage of the study was the study of indicators of Ultrasound investigation of BCV in pregnant women with a physiological course, as well as with mild and severe preeclampsia, in a comparative aspect (table. 1.).

Table 1. Indicators of the ultrasound diagnosis of brachio-cephalic vessels in a comparative aspect in the groups studied at admission

	Physiological pregnancy	Mild pre-eclampsia	Severe pre-eclampsia	Normal performance
Diameter of blood vessels				
POSA	7.5	7.45	5.55	5-8 mm
LOSA	6,6	6.8	5.1	5-8 mm
PPA	2.2	1.75	1.55	2-3 mm
LPA	2.3	1.9	1.55	2-3 mm
Blood flow velocity				
POSA				
Vps	56	68	77.5	50-80 cm/s
Wed	25	26	38	25-30 cm/s
RI	0.9	0.95	1.35	0.8-1.0 cm/s
PI	1.1	1.45	1.85	1.0-1.5 cm/s
LOSA				
Vps	54	65.5	76.5	50-80 cm/s
Wed	29	29.5	33.5	25-30 cm/s
RI	0.9	0.9	1,3	0.8-1.0 cm/s
PI	one	1.35	1.7	1.0-1.5 cm/s
PPA				
Vps	39	56	59	30-50 cm/s
Wed	sixteen	26	28	15-25 cm/s
RI	0.8	1,3	1.8	0.8-1.0 cm/s
PI	1.1	1.75	2.05	1.0-1.5 cm/s
LPA				
Vps	37	52.5	53.5	30-50 cm/s
Wed	18	24	27.5	15-25 cm/s
RI	0.9	1.4	2.1	0.8-1.0 cm/s
PI	1,3	1.75	2.3	1.0-1.5 cm/s

There is an increase in the velocity indices of the vascular blood flow, as the degree of preeclampsia progresses. A narrowing of the lumen (diameter) of the vessel, as the degree of preeclampsia progresses, is also noted. In addition, a marked increase in speed indicators mainly in the vertebral arteries. Also marked increase in indicators: RI, PI.

These pregnant women, subdivided into groups, studied endothelial dysfunction indicators, examining the state of von Willebrand blood (WF) and Asymmetric dimethylarginine (ADMA). This study was conducted for a

comparative analysis of these indicators between physiological pregnancy, as well as preeclampsia (including mild and severe preeclampsia).

The factor Willebrand factor (WF) in pregnant women from the main group, in a subgroup of women with preeclampsia Mild grade was normal in 4 (40%) women, and there was an increase in performance in 6 (60%) pregnant women. On average, the rate indicator was equal to 109.5. And the raised indicator was on average equal - 172.2. And in the subgroup with severe preeclampsia, the rate was normal in 3 (30%) women, and there was an increase in rates in 7 (70%) pregnant women. On average, the rate indicator was equal to - 120.3. And the raised indicator was on average equal - 196.3.

Asymmetric dimethylarginine (ADMA) in pregnant women of the main group, in the subgroup with mild preeclampsia, was normal in 5 (50%) women, and in 5 (50%) patients there was an increase in this indicator. The norm indicator was on average equal to 113.4. And the raised indicator was on average equal - 185.2. And in the subgroup with severe preeclampsia, it was normal in 2 (20%) women, and in 8 (80%) patients there was an increase in this indicator. The average rate was on average - 115. And the raised indicator was on average equal - 211.8. According to the results of our own research, we can conclude that pregnant women with preeclampsia have neurological symptoms, which increases with the progression and severity of preeclampsia. Accordingly, the complaints of patients with the nervous system also increase depending on the degree of preeclampsia.

If we talk about electroencephalography indices, it can be concluded that during pregnancy with mild and severe preeclampsia, pathological changes in the cerebral cortex are observed, prone to convulsive and epileptiform activity, by the interest of deep structures, depending on the degree of preeclampsia, that is the more pronounced the degree of preeclampsia, the more severe the changes in the EEG indices are characteristic, which is not observed during the physiological course of pregnancy. Based on the data shown above, by the ultrasound diagnosis of brachio-cephalic vessels, it can be concluded that in this category of patients, the total CIM does not change, the vascular geometry is not changed, there is no deformation of the BCV, extravasal pressure, and also no plaques are noted. There is an increase in the velocity indices of the vascular blood flow, as the degree of preeclampsia progresses. A narrowing of the lumen (diameter) of the vessel, as the degree of preeclampsia progresses, is also noted. In addition, a marked increase in speed indicators mainly in the vertebral arteries. Also marked increase in indicators: RI, PI. Analyzing the results of laboratory data, it can be concluded that during physiological pregnancy the level of endothelial dysfunction factors like von Willebrand Factor (FW) and Asymmetric Dimethylarginine (ADMA) do not increase, which in turn indicates normal functioning of the vascular endothelium. And with preeclampsia, depending on the severity, these indicators also increase accordingly, which indicates the damage to the vascular endothelium in this pathology of pregnancy.

It is equally important to emphasize that there is a strong correlation between the manifestations of clinical and neurological changes, as well as a laboratory of ofatorno-biochemical parameters (FW, ADMA) and the data of functional diagnostic methods (EEG, Ultrasound investigation of BCV). In turn, these findings help us to identify the risk group in pregnant women with mild preeclampsia for a possible transition to severe preeclampsia, as well as selection of pregnant women among this cohort for possible development of cerebrovascular pathology during pregnancy, childbirth, and the postpartum period. What makes it possible to select the correct management of pregnancy and childbirth, and thus the treatment, as well as the prevention of cerebrovascular disease in the future.

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