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MODERN ASPECTS OF PREDICTING PREMATURE BIRTH

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Premature birth (PB), today, is a major problem in obstetrics and perinatology not only in Ukraine but around the world. Investigation of miscarriage problems and understanding of the main links of its pathogenesis are one of priority directions of modern obstetrics. Rate of this pathology takes almost 30 % and doesn't trend to decrease. It has direct influence on demographic situation in countries all over the world [1, 2].

The urgency of the problem of PB is due to at least two factors. The first is a significant share of prematurity in the structure of perinatal and infant mortality: 70% of all cases of neonatal mortality and 36% of infant mortality occur in premature newborns. This factor is gradually losing its significance, because the success of modern neonatology has increased the survival rate of premature infants up to 80-90% [3]. In 2018, it was 3.7% in the Zaporozhye region, and according to the statistical data of the PI «Zaporozhe Regional Perinatal Center» - 13.0%. However, it should be noted that the high rate at this medical institution is due to the specific orientation and the contingent of patients seeking for medical care. That is why the problem of stillbirth

requires a detailed study of how to prevent as miscarriages, as PB and birth of children with a low birth weight [4].

Despite the continuous improvement of neonatal services, which constantly increase the survival rate of premature babies, infant morbidity and mortality can be affected only by early detection and formation of risk groups for PB among pregnant women and choosing an effective strategy to prevent this condition.

The contingent of surveyed and research methods

63 patients participated in the gestation period of 22-34 weeks in a prospective open study. Pregnant women were divided into two groups. Thus, the first group included 44 pregnant women, with the threat of PL, and the second group included 19 patients with normal course of pregnancy.

All women were tested for body mass index (BMI), progesterone, insulin and cortisol on the day of admission.

Statistical processing of materials was carried out by using the software package "Statistica 13.0" and MedCalc. 10.2.0.0. To determine the predictors of the occurrence of a TPL, the method of binary logistic regression analysis was used. All statistical tests were two-sided; the p-0.05 level was considered as significant.

Research results and their discussion

Pregnant women with TPL accounted for 70% (44 out of 63 pregnant women) of the total number of patients involved in the study. For 12 women, pregnancy ended with preterm birth, accounting for 19% of the total. Most pregnant women (81%) gave birth in full-term pregnancy.

According to the results of the study, pregnant women with TPL had a 57% (p <0.05) greater duration of hospital stay after germination in comparison with women with normal course of pregnancy (6.9 ± 1.27 days versus 3.7 ± 0. 33 days). This was due to the premature birth and in some caces the need for special medical care for preterm infants and resuscitation measures. In the structure of diseases of preterm infants, the leading ones were: hypoxic-ischemic injury of the central nervous system with inhibition syndrome, neonatal jaundice, respiratory distress syndrome, predominantly Type I, intraventricular cerebral hemorrhages and retinopathy of preterm ones. Two children had a congenital heart disease as an intraventricular septum defect and an atrial septum defect, 2 children had neonatal jaundice. Proved is the fact that the consequences of non-carrying of pregnancy for the mothers organism are infection of the uterus, associated with it courses of antibiotic therapy, disorders of lactation regulation, etc. [5]. Thus, according to scientific literature, TPL and prolongation of stay in a hospital due to premature births, preterm infants who require high-quality medical care from the first minutes of life are associated with the lack of a perfect scheme of therapy, prevention of TPL and the premature births itself [6]. Significance of the absence of a unified treatment scheme for TPL can be underlined by the high level of occurrence for this pathological condition, prolongation of the length of stay in the hospital, the need for intensive care, complications and (indirectly) an increase in the cost of treatment. PB is the main cause of perinatal morbidity and mortality, which accounts for up to 80% of deaths of newborns. However, a high mortality rate persists among those, who were born in 32-36 weeks of gestation. In children born prematurely, survivors are determined by a number of adverse neonatal

diseases: chronic pulmonary disease, retinopathy of preterm newborns, traumatic brain injury, necrotic enterocolitis and neonatal sepsis.

In spite of the continuous improvement of neonatal services, which constantly increase the survival rate of early premature children, it is possible to influence the incidence and mortality of infants only by early detection, formation of a risk group of TPL among pregnant women and the selection of an effective prevention strategy for this condition.

In order to find out the factors that influence the course of pregnancy and increase the risk of premature birth, we have conducted an analysis of the results from the monitoring of 63 pregnant women who were observed in the PI "Zaporozhye Perinatal Center". To determine the cut-off value of quantitative indicators that increase the risk of TPL, ROC analysis was used. We obtained the following distribution points for a number of indicators: the age of pregnant women over 25 years (sensitivity 70.5%, specificity 68.4%, area under the ROC curve 0.638 (95% CI 0.507- 0.755, p = 0, 0594)); body mass index (BMI) ≤ 24 kg / m² (sensitivity 47.7%, specificity 89.5%, area under the curve 0.623 (95% CI 0.492- 0.742, p = 0.1207)); Insulin> 8.65 μMe / ml (75% sensitivity, specificity 63.2%, area under the curve 0.665 (95% CI 0.535-0.779; p = 0.02), cortisol ≤ 577.9 ng / ml (sensitivity 56, 8%, specificity 84.2%, area under the curve 0.665 (95% CI 0.524- 0.770, p = 0.05), progesterone ≤ 139.5 ng / ml (sensitivity 34.1%, specificity 89.5%), area under the curve of 0.572 (95% CI 0.441-0.606; p = 0.37)). By using logistic regression analysis, predictors of the threat of premature birth were identified. Factors that had a probable predictive value in one-factor analysis were further included in the multivariate model for the determination of independent predictors.

Consequently, all the above-mentioned indicators were included in the dependent predictors of the occurrence of TPL. They were: Body Mass Index (BMI) ≤ 24 kg / m² significantly increased the odds ratio (OR) of TPL at 7.76 times (95% CI 1,598-37,683; p = 0.011); the level of insulin <8.65 μM / ml significantly increased OR of the TPL in 5.14 times (95% CI 1.62-16.328; p = 0.004); the OR of TPL increased in 7.02 fold (95% CI 1,784-2612; p = 0.001) in case that the cortisol level was less than 577.9 ng / ml; the progesterone level <139.5 ng / ml increased the odds ratio of TPL in 4.39 times (95% CI 0.8945 - 21.608; p = 0.0683).

According to the models of multivariate logistic regression analysis, independent factors which increase the risk of TPL are: age of pregnant women over 25 years, body mass index ≤ 24 kg / m², blood insulin level> 8.65 μMe / ml, blood cortisol in serum $\leq$ 577.9 ng / ml and progesterone ≤ 139.5 ng / ml.

Consequently, the TPL association with the age of pregnant women over 25 years significantly increases the odds ratio of premature infusion in 5.17 times, which may be the result of gradual depletion of maternal body, aging of the sex cells, prolonged influence of pathogens and toxic substances, and the presence and exacerbation of chronic pathology.

According to some authors, primipara women of the older age group, namely at the age over 35, have a high risk of PB, untimely rupture of amniotic membranes, clinically contracted pelvis, soft tissue ruptures, pathological blood loss in labor and very high

risk of development of discoordination of the delivery forces and asphyxia of newborns [7, 8].

Interesting is the fact that weight deficiency, concretely BMI ≤ 24 kg / m2, significantly increases the risk of non-carrying of pregnancy in 7.76 times.

According to our data, the unconditional effect on TPL results insulin level in serum. So, according to our study, an increase of insulin level more than 8.65 μM / ml increases the odds ratio of TPL in 5.14 times.

The odds ratio of TPL, according to our results, increases in 7.02 times in case that the reduction of cortisol level is below the limit of 577.9 ng / ml.,appears is, namely the initial increase in the content of cortisol with subsequent inhibition of its level on the background of the depletion of energy reserves.In our opinionin pregnant women, who are in a state of chronic stress, this fact is combined with a two-phase response of the adrenal glands on the pathological stress effect, namely the initial increase of cortisol with subsequent inhibition of its level against the background of the depletion of energy reserves.

After weighing the data of the univariate regression analysis, multivariate models of independent predictors of TPL were created.

According to the first model (p = 0.0001), independent factors of risk of miscarriage include:

- the age of a pregnant women over 25 years - increases the OR of TPL in 4.2 times (95% CI, 1.12 - 15.50, p = 0.03);

- the insulin level more than 8.7 - increases the OR of TPL in 4.4 times (95% CI 1.16 - 16.24; p = 0.03);

- the cortisol level less than 577.9 - increases the OR of TPL in 5.1 times (95% CI 1.35 - 25.80; p = 0.02).

According to the second model (p <0.0001), independent risk factors for increasing the risk of TPL are:

- BMI less than 24 kg / m2 - increases the chance of a risk of threatening in 24.8 times (95% CI 3.00 - 204.01; p = 0.002);

- the level of insulin more than 8.7 - increases the OR of a threat of non-carrying of pregnancy in 11.2 times (95% CI 2.02 - 62.37; p = 0.005);

- the level of cortisol is less than 577.9 - increases the chances of a risk of miscarriage in 13.1 times (95% CI 2.19 - 77.95; p = 0.004).

However, the most interesting is the third model (p <0,0001) of independent risk factors for TPL of course. It includes four indicators:

- the level of progesterone less than 139.5 - increases the chances of TPL in 8.2 times (95% CI 1.06 - 63.94; p = 0.043);

- the level of cortisol less than 577.9 - increases the odds ratio of chances of the risk of miscarriage in 10.6 times (95% CI 1.93 - 57.68; p = 0.006);

- BMI less than 24 kg / m2 increases the OR of risk of threatening of pregnancy in 4.5 times (95% CI 1.89 - 81.14; p = 0.008).

Conclusions

The results from the conducted research clearly show that the use of multivariate logistic regression analysis allowed to determine the predictors of threatened premature

birth. Taking into account the obtained data, it was found that among pregnant women with a threat of preterm labor the most informative are age and BMI, and in combination with the hormonal examination of women are of primary importance.

The obtained results indicate the expediency of inclusion to the standard examination of pregnant women with a threat of premature birth, a comprehensive determination of the level of progesterone, insulin and cortisol, which will enable to identify the risk group for this complication in time and to propose preventive measures.

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