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Original Article

Innovative markers for the diagnosis of preeclampsia and their role in the management of treatment in obstetric practice

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Abstract

The relevance of preeclampsia during pregnancy is due to its significant impact on the health of both the mother and the fetus. To explore the features of diagnosing novel markers of preeclampsia, particularly inhibin A, and assess their role in the management of treatment in obstetric practice, with an emphasis on predicting the development and severity of preeclampsia. Neural network methods were also applied to improve predictive results, particularly the decision tree model (data mining), which enabled the identification of important factors influencing the development of pathologies in pregnant women. The study highlights serious pregnancy complications in women at high risk of preeclampsia, particularly hemodynamic disorders in the uterine arteries and elevated levels of inhibin A, which may serve as an early marker for the diagnosis of preeclampsia. Women who received modified pathogenetically justified treatment showed better pregnancy outcomes compared to those receiving standard therapy. A comparison of the first and second study groups showed that women who received modified pathogenetically justified treatment had significantly better pregnancy outcomes compared to those who received standard therapy. In the high-risk group, there was a significantly higher incidence of complications, including hemodynamic disorders in the uterine arteries, the onset of preeclampsia, and preterm labor. With the development of new technologies, innovative markers have emerged that allow for early detection of this condition, enhancing the possibilities for personalized treatment.

Keywords: preeclampsia, inhibin A, decision tree, diagnosis, treatment

Introduction

Preeclampsia remains one of the leading causes of maternal and perinatal mortality worldwide, affecting 2–8% of pregnancies. Timely diagnosis and effective treatment are crucial for reducing pregnancy complications, such as preterm birth, stroke, and heart failure in the mother. Since this condition is associated with serious long-term health consequences for the mother, including an increased risk of cardiovascular diseases, the relevance of preeclampsia research remains extremely high. The development of new methods for early diagnosis based on biomarkers and personalized screening algorithms is an important step in preventing this condition and improving pregnancy outcomes [1, 2].

The relevance of preeclampsia during pregnancy is due to its significant impact on the health of both the mother and fetus, as well as its high prevalence worldwide. Recent studies indicate an increasing frequency of preeclampsia, associated with several factors, such as lifestyle changes, a higher average age of women giving birth, and an increase in cases of obesity and

comorbid conditions. This issue requires timely diagnosis and effective treatment, as early detection and risk management can significantly improve pregnancy outcomes [3, 4].

It is also important to emphasize that the presence of preeclampsia can have long-term health consequences for women, including an increased risk of cardiovascular diseases later in life. In this regard, research on the causes, mechanisms, prevention, and treatment of preeclampsia is critically important for improving perinatal outcomes and women's health in general [5, 6].

Studies conducted suggest a possible link between maternal iron levels and the risk of developing preeclampsia or eclampsia. However, despite these observations, the causal relationship between these factors remains unclear and requires further investigation. Scientists are still unable to confidently assert whether iron deficiency is a direct cause of these serious conditions or if it is more of an observed correlation that requires additional research for confirmation [7, 8].

There is a difference in complications for pregnant women with early-onset preeclampsia compared to those who develop it later. Women with moderate preeclampsia typically experience adverse outcomes for both mothers and newborns [9, 10].

The development of preeclampsia during pregnancy is associated with numerous risk factors that can affect the health of both the mother and fetus. First and foremost, women experiencing their first pregnancy are at an increased risk of developing this complication. A significant aspect is medical history: the presence of preeclampsia in previous pregnancies significantly increases the likelihood of recurrence. The age of the pregnant woman is also a critical factor, as women over 35 are more susceptible to developing preeclampsia. Multiple pregnancies, malnutrition, genetic factors, endocrine disorders, complicated obstetric and gynecological history, inflammatory diseases of the genital tract, and cardiovascular diseases can increase the risk and complicate the course of pregnancy [11–13].

As of today, there is no doubt that preeclampsia is associated with a systemic inflammatory response, endothelial dysfunction, and an imbalance of angiogenic and anti-angiogenic factors, as well as metabolic disorders. The search for effective methods for diagnosing preeclampsia in pregnant women is one of the most pressing issues in modern obstetrics. As of now, the etiological factors and markers of preeclampsia remain unknown. The rate of progression of pathological changes, as well as treatment and prevention options for this condition, are limited and insufficiently studied. The development of prognostic criteria will allow for the prediction of preeclampsia development in late pregnancy, facilitating the identification of a group of patients requiring close monitoring due to a high risk of complications. Timely diagnosis will enable the initiation of prevention measures for intrauterine complications of the fetus, which will reduce the number of cases requiring neonatal resuscitation. In placental ischemia, there is a noted imbalance of placental markers, such as pregnancy-associated plasma protein-A and inhibin A [14–16].

During placental ischemia, an increase in the level of the placental marker—inhibin A—is observed. Inhibin is a heterodimer consisting of two subunits: alpha (α) and beta (β), with the β-subunit existing in two variants—A and B. Inhibin selectively inhibits the secretion of follicle-stimulating hormone by the pituitary gland, whereas activin, on the contrary, stimulates its production. In women, these proteins play an important role in reproductive processes. Inhibin is synthesized not only by the gonads but also by the pituitary gland, adrenal glands, and placenta.

Material and methods

General clinical examination methods for pregnant women were used, along with biochemical and statistical research methods. Statistical analysis of the obtained data was conducted, calculating the mean (M) and standard error (m). The study section also utilized machine learning methods, particularly neural networks, to enhance the prediction and analysis of results. One of the applied methods was the decision tree model, which allowed for the identification of important factors and their impact on the development of pathologies in pregnant women.

The decision tree method was used to construct predictive models based on input clinical and biochemical data. This model enables a hierarchical distribution of various risk factors and assists in predicting the likelihood of certain complications occurring during pregnancy. Each node of the tree is responsible for making a decision regarding further analysis based on the value of one or more indicators, while each branch represents the possible outcomes depending on that decision. To train the neural network and build the decision tree, appropriate algorithms were utilized in the Statistica 10.0 and Microsoft Office Excel 2016 software packages, as well as Python machine learning libraries.

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Results

In the study, three groups of pregnant women were formed with different treatment protocols: Group I: This group included 31 women who were classified as high-risk for developing preeclampsia. Patients received modified therapy that included protocol treatment along with vitamin D supplementation at a dose of 2000 IU, L-arginine at 3000 mg, calcium carbonate at 1000 mg, magnesium sulfate at 1000 mg, and acetylsalicylic acid at a dose of 75 mg per day. Group II: This group consisted of 38 women whose pregnancies were complicated by moderate preeclampsia; these patients received standard protocol therapy without additional modifications. Group III: This group included 40 women who experienced physiological pregnancies without complications or extragenital pathology. Such a division into groups allows for a comparison of the effectiveness of different approaches to treating preeclampsia and an assessment of the impact of additional therapeutic measures in patients.

To diagnose the development of preeclampsia in our study, we focused on determining the level of inhibin A. This marker is an important indicator that allows for the assessment of the risk of developing this complication during pregnancy. Inhibin A is known to play a key role in regulating a woman's hormonal background, and its level can vary significantly depending on the mother's health and the development of the fetus. Measuring this marker enables not only the detection of early signs of preeclampsia but also timely treatment adjustments, which are critical for the health of both the mother and the child.

At 16–18 weeks' gestation, the level of inhibin A was measured in all patients in the studied groups, as appears in Figure 1.

The analysis of the significance of differences in the levels of inhibin A among the different groups showed significant results. Specifically, a p-value of 0.041 indicates a statistically significant difference between the first and second groups, which suggests variability in the levels of inhibin A in pregnant women with preeclampsia in the context of metabolic syndrome. Moreover, between the second and third groups, there was a high level of significance in the differences, with a p-value of 0.001, confirming the difference in inhibin A levels in women with physiological pregnancies. A statistically significant difference was also found between the first and third groups, with a p-value of 0.001. The obtained data emphasize the varying levels of inhibin A in pregnant women with different degrees of risk for developing preeclampsia, underscoring the importance of this marker for diagnosing potential complications during pregnancy. In patients from the third control group, the level of inhibin A at 16–18 weeks of gestation was significantly lower than in women from the high-risk group for developing preeclampsia.

The course of pregnancy, within the framework of the prospective study, turned out to be significantly worse in patients from the high-risk group for developing preeclampsia compared to the control group. In women from the second studied group, cases of placental insufficiency, preterm labor, and preeclampsia were more frequently observed, along with a higher incidence of preterm deliveries.

The study showed that the course of pregnancy and childbirth in women from Group II was significantly more severe compared to the control group. The analysis also confirmed that patients who received modified pathogenetically justified treatment had better pregnancy outcomes than those who received only standard therapy. In women from Group I, hemodynamic

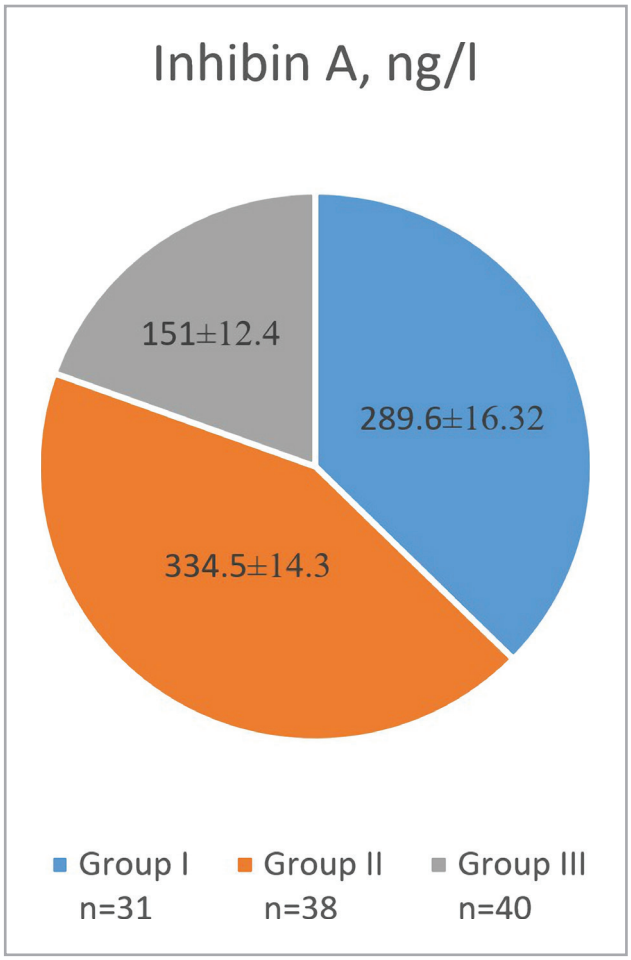

Figure 1: The level of inhibin A in pregnant women belonging to the high-risk group for developing preeclampsia at 16-18 weeks of pregnancy.

Table 1: Pregnancy complications in women of the study groups.

Group I	Group II
Preeclampsia	**Preeclampsia**
Yes (25.8%)	Yes (50%)
Hemodynamic disturbances	**Hemodynamic disturbances**
Yes (22.5%)	Yes (34.2%)
Preterm labor	**Preterm labor**
Yes (25.8%)	Yes (10.5%)

disturbances in the uterine arteries were recorded in 22.5% of cases, preeclampsia occurred in 25.8%, and preterm labor was noted in 25.8%. During the analysis, it was found that in Group II, the frequency of complications was higher: hemodynamic disturbances in the uterine arteries were detected in 34.2%, preeclampsia in 50%, and preterm labor in 10.5% of patients, as appears in Table 1.

The decision tree method is a decision-making tool used in statistical analysis and data processing with the help of artificial intelligence. The main idea of the method is to build a mathematical model that defines the relationship of the target variable (the factor being studied) with other independent variables and allows for the prediction of the probability of its value. If the target variable has discrete values (for example, "yes" or "no"), the decision tree method helps establish its relationship with other variables and solve the forecasting task.

At each stage, the decision tree shows different scenarios for patients based on their group and the presence of specific complications. This decision tree helps visualize the risks in patients depending on their group and existing complications.

Discussion

Considering the stable indicators in women with uncomplicated pregnancies, an increase in the level of inhibin A, which can be easily determined in practice, may serve as a marker for identifying patients who fall into the risk group for developing preeclampsia. Therefore, it is advisable to analyze this marker at 16–18 weeks of pregnancy to ensure early diagnosis, prevention, and treatment of preeclampsia in women with metabolic syndrome.

The course of pregnancy, within the framework of the prospective study, turned out to be significantly worse in patients from the high-risk group for developing preeclampsia compared to the control group. In women from the second studied group, cases of placental insufficiency, preterm labor, and preeclampsia were more frequently observed, along with a higher incidence of preterm deliveries [17, 18].

The analysis of clinical and anamnestic data, as well as obstetric and perinatal outcomes within this study, confirmed the importance of medical history in determining the risk of developing preeclampsia, which is significant for practical activities. At the same time, the insufficient predictive accuracy of these factors highlights the need for further research to identify modern molecular-genetic and immunological predictors of preeclampsia, focusing on early diagnosis and assessment of the severity of this condition.

Conclusions

The conclusions of this study underscore the serious complications associated with pregnancy in women at high risk for developing preeclampsia. A comparison of the results between Groups I and II indicates that women who received modified pathogenetically justified treatment had significantly better pregnancy outcomes compared to those who underwent only standard therapy. In the high-risk group, the frequency of complications was considerably higher, with significant occurrences of hemodynamic disturbances in the uterine arteries, preeclampsia, and preterm labor observed in a substantial portion of patients.

The study confirms the importance of early diagnosis and effective treatment in pregnant women with risk factors. The differences in complication rates between the groups indicate the necessity for an individualized approach to managing pregnancies, which can reduce risks for mothers and their children. Consequently, further research should focus on developing

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and implementing new therapeutic strategies to improve pregnancy outcomes in women at increased risk for developing preeclampsia.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Ethics Committee of the Ternopil National Medical University, Ternopil, Ukraine (approval ID: protocol No. 5, dated September 1, 2021).

Consent to participate

Written informed consent was obtained from all the participants.

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