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Prediction of ovarian masses in pregnant women

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ABSTRACT

BACKGROUND: Ovarian masses during pregnancy are a common pathology, occurring in up to 3.2% of cases. However, data on recurrence after the removal of ovarian masses in women, which could help predict their potential occurrence, remain limited.

AIM: To assess the feasibility of predicting ovarian masses during pregnancy through a prognostic model based on data obtained using developed scoring systems.

MATERIALS AND METHODS: The study included 100 women in their second and third trimesters of pregnancy, divided into two groups: group 1 (main group) consisted of 50 pregnant women with ovarian masses that appeared for the first time (before the first delivery) or recurred (before the second delivery); group 2 (control group) included 50 pregnant women without ovarian pathology in either their first or subsequent pregnancies.

RESULTS: Two prognostic models were developed and tested on a random sample of 24 pregnant women with newly diagnosed or recurrent ovarian masses. The accuracy of the predictions was found to be acceptable, with a predictive accuracy of 83% in the first case and 62% in the second.

CONCLUSION: Prognostic models appear feasible for estimating the probability of both newly diagnosed and recurrent ovarian masses. This approach enhances diagnostic accuracy, improves prevention strategies for gynecological pathology, and aids in the selection of appropriate treatment and management strategies for patients with ovarian masses, even before ultrasound evaluation or surgical intervention.

Keywords: ovarian masses; pregnancy; cervical insufficiency; spontaneous abortion; myopia; obesity.

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Возможность прогнозирования возникновения образований яичников у беременных

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АННОТАЦИЯ

Обоснование. Образования яичников во время беременности являются часто встречаемой патологией и достигают 3,2%. Однако в литературных источниках мало данных о рецидивах после удаления образований яичников у женщин, которые могли бы предсказать их возможное возникновение.

Цель. Оценка прогнозирования возникновения образований яичников у женщин во время беременности в виде прогностического правила на основании данных, полученных с помощью разработанных шкал.

Материалы и методы. В исследование вошли 100 женщин во втором и третьем триместрах беременности. Они были разделены на две группы: 1-я (основная) — 50 беременных с образованиями яичников, возникшими как впервые (перед первыми родами), так и повторно (перед вторыми родами); 2-я (контрольная) — 50 беременных без патологии как при первой, так и при повторной беременности.

Результаты. В ходе исследования были сформированы два прогностических правила, которые использовали на тестовой выборке случайно взятых 24 беременных с впервые и повторно возникшими образованиями яичников. Совпадение прогноза с реальным состоянием дел оказалось вполне приемлемым, степень прогноза в первом случае составила 83%, во втором — 62%.

Заключение. Применение прогностических правил является вполне возможным для диагностики оценки вероятности развития как впервые, так и повторно возникших образований яичников. Такой подход увеличивает точность диагностики, профилактики гинекологической патологии, а также помогает выбрать методы лечения и ведения пациенток с образованиями яичников ещё до УЗИ или оперативного вмешательства.

Ключевые слова: опухоли яичников; беременность; истмико-цервикальная недостаточность; аборт; миопия; ожирение.

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妊娠期卵巢肿块发生的预测可能性

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摘要

背景。妊娠期卵巢肿块是一种常见病理状况，其发生率可达3.2%。然而，现有文献中关于卵巢肿块切除术后复发的研究较少，而这些数据可能有助于预测其再次发生的可能性。

目的。评估基于评分量表数据建立预测规则的可行性，以预测妊娠期卵巢肿块的发生。

材料与方法。本研究纳入100名妊娠中晚期的女性，并分为两组：第1组（研究组，n=50）妊娠期发生卵巢肿块，包括初次发生（首次妊娠前）及复发（再次妊娠前）；第2组（对照组，n=50）无卵巢肿块病史的妊娠女性（既往妊娠及当前妊娠均未出现病变）。

结果。研究建立了两个预测模型，并在随机选取的24例妊娠期首次或复发性卵巢肿块患者中进行了测试。预测结果与实际情况的符合率较高，首次发生病例的预测准确度为83%，复发性病例的预测准确度为62%。

结论。预测模型的应用可用于诊断评估妊娠期卵巢肿块的首次及复发性发生风险。这种方法提高了卵巢病变的诊断和预防准确性，同时有助于在超声检查或手术干预之前选择合适的治疗和管理策略。

关键词： 卵巢肿块；妊娠；峡部-宫颈机能不全；流产；近视；肥胖。

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BACKGROUND

Ovarian masses are the most common pathology in pregnant women [1], of which 60%–70% are benign and 33% are tumor-like [2]. According to the study by Zahra [3], the mean age of detection for ovarian masses was 32 years. Epithelial tumors were identified in 39.5% of patients, functional cysts in 32.1%, germ cell tumors in 17.3%, and in rare cases, sex cord-stromal tumors [1, 2].

The incidence of ovarian masses during pregnancy reaches 3.2% [4], some of which resolve within 2–4 months without intervention [5]. There are few data on the possibility of recurrence after the removal of ovarian masses in women. For example, in the study by Davydov et al. [6], the probability of ovarian tumor recurrence was 10%–14%.

The study aimed to assess the feasibility of predicting ovarian masses during pregnancy through a prognostic model based on data obtained using developed scoring systems.

METHODS

Wald sequential analysis, a standard approach in medical research [7, 8], was employed to create the rule. The data from two groups of pregnant women, obtained from anamnestic and laboratory analyses, were used to support this prediction. For this purpose, sociobiological and instrumental indicators, obstetric and gynecological and somatic history, information on concomitant extragenital pathology, the process of delivery and details of the child's condition at birth and in the early neonatal period were used. The data were collected through a retrospective analysis of prenatal, delivery, and neonatal records of 100 women in the second and third trimesters of pregnancy, as well as in the postpartum period.

Group 1 (main group) consisted of 50 women diagnosed with ovarian masses that appeared for the first time (before the first delivery) or recurred (before the second delivery). Group 2 (control group) included 50 pregnant women without ovarian pathology in either their first or subsequent pregnancies. In order to predict the prognosis of recurrent ovarian masses, group 1 was divided into two subgroups. Subgroup 1 comprised 34 cases of no cyst in repeat pregnancy, whereas subgroup 2 comprised 16 cases of both primary and secondary occurrence of ovarian masses. All the obtained anamnestic and laboratory data were entered into an Excel attribute table, thereby forming a profile of group description. This profile was then subjected to mathematical and statistical analysis using modules of the Statistica 10 software package [9].

At the first stage, all anamnestic and clinical data were sequentially tested for risk factors. The method of Wald sequential analysis is based on the use of nominal (categorical, alternative) variables. For most of the anamnestic data, this was self-consistent. However, the indicators that were the result of precise measurements (sizes and concentrations) had to be converted into nominal values. The boundaries were defined within the range of variation to distinguish intervals of values that could be considered as belonging to normality or pathology. In cases where such separation was not possible, the distribution was analyzed using histograms to detect bipolarity or the ranges of values separated by an "empty" interval. These ranges were thus considered and subsequently labeled as discrete categories.

Subsequently, the reliability of the association between the gradations of a characteristic that could be considered a risk factor and the patients' belonging to the group with ovarian masses or to the control group, as well as to the group with the newly diagnosed or recurrent pathology, was evaluated. This evaluation was conducted by employing Pearson χ^2 criterion and Fisher nominal correlation coefficient φ [10]. If there was a reliable association and the coefficient φ was at least in the moderate range (⩾0.3), the variable was considered a potential risk factor. Standard formulas [11] were used to calculate odds ratios (OR), which indicate how often an event is more likely to occur in one group than in another. A confidence interval for this parameter was then constructed. The analysis was conducted with the exclusion of parameters for which the lower limit of the OR confidence interval was <1. The diagnostic coefficients (DC) for the presence (DC_+) and absence (DC_-) of a risk factor were then calculated using the data from the four-fold tables obtained by calculating OR and χ^2 [7, 8].

At the second stage of the study, the obtained prognostic tables were tested on a random sample of 24 pregnant women.

RESULTS

In the course of the described procedures, two prognostic rules were created.

Prognostic Rule for Evaluating the Newly Diagnosed Ovarian Masses in Pregnant Women

The analysis of the 61 variables that constituted the descriptive profile of the group of pregnant women with ovarian masses (group 1) and without pathologies (group 2) resulted in the identification of eight variables that met the above criteria. These elements are ranked by their OR level (Table 1).

1. **Abortions before childbirth:** yes or no.

χ^2=34, φ=0.57, p < 0.0001; OR=13.6 (5–36); DC_+=+7, DC_-=–5.

2. **Menstrual cycle disorders**: yes or no.

χ^2=17.9, φ=0.40, p < 0.0001; OR=13 (3–62); DC_+=+4, DC_-=–8.

3. **Endometriosis**: yes or no.

χ^2=13.3, φ=0.35, p < 0.0003; OR=10 (2.2–48.0); DC_+=+3, DC_-=–7.

4. **Dysmenorrhea**: yes or no.

χ^2=9.0, φ=0.3, p < 0.003; OR=9 (1.4–36.0); DC_+=+3, DC_-=–6.

5. **Myopia**: yes or no.

χ^2=22, φ=0.46, p < 0.0001; OR=8.5 (3.2–22.5); DC_+=+4, DC_=–5.

6. **Less than four pregnancies**: yes or no.

χ^2=20.7, φ=0.44, p < 0.0001; OR=7 (2–17); DC_+=+5, DC_=–4.

7. **First childbirth only**: yes or no.

χ^2=9.2, φ=0.30, p < 0.002; OR=3.9 (1.6–9.6); DC_+=+3, DC_=–3.

8. **Obesity of any degree**: yes or no.

χ^2=8.9, φ=0.30, p < 0.003; OR=3.7 (1.5–9.0); DC_+=+3, DC_=–3.

Since this pilot study was only designed to test the ability to predict ovarian masses, the acceptable first (α) and second (β) type error probabilities were set at 0.05 and 0.1, respectively. The decision thresholds for the diagnostic rule were established at +9.8 and –12.6, or +10 and –13 after rounding. According to the publications [12], the recurrence rate of ovarian masses varies between 0.5%–3.4%. The highest estimate of 3.4% has an a priori DC of –14, the lowest estimate of 0.5% has an a priori DC of –22, and the moderate estimate of 1.5% has an a priori DC of –18. We used the most optimistic estimate of 3.4% and an a priori DC of –14. Consequently, if the algebraic sum of the a priori DC and all DC_+ and DC_ exceeds the threshold of 10, taking into account all the presented risk factors, a recurrence of ovarian masses in pregnant women should be expected with 95% probability. If the sum is less than –13, there is a 90% probability that recurrence will not occur. If the sum falls within the thresholds of the diagnostic rule, a prognosis becomes impossible due to the inability to reach a definitive decision with a high degree of certainty. Obviously, the prediction in this case depends significantly on which of the a priori DCs is considered the most realistic. This is due to the observed differences in the estimates of the probability of cyst occurrence among published studies, which exhibit a range that is nearly an order of magnitude apart.

Table 1. Prognostic table for assessing the risk of ovarian masses in pregnant women

Risk factors	Gynecological history	Somatic pathology
Abortions before childbirth		
Yes	+7	–
No	–5	–
Menstrual cycle disorders		
Yes	+4	–
No	–8	–
Endometriosis		
Yes	+3	–
No	–7	–
Dysmenorrhea		
Yes	+3	–
No	–6	–
Myopia		
Yes	+4	–
No	–5	–
First childbirth only		
Yes	+3	–
No	–3	–
Less than four pregnancies		
Yes	+5	–
No	–4	–
Obesity of any degree		
Yes	–	+3
No	–	–3

The resulting prognostic table was tested on a sample of random 24 pregnant women. Twenty women had an algebraic sum of all parameters <–13 and four women had >–13 but <+10. Medical history analysis showed that all of these women did not have ovarian masses in subsequent pregnancies. Specifically, the prognosis was consistent with the actual outcome in 20 out of 24 cases, and its true reliability was 83%.

Prognostic Rule for Evaluating the Recurrent Ovarian Masses in Pregnant Women

The analysis of 115 variables that constituted the descriptive profile of the group of pregnant women with and without recurrent ovarian masses resulted in the selection of seven variables that satisfied the above criteria. The ranking of these elements is determined by their OR level (Table 2).

1. **Abortion before the second childbirth**: yes or no.

χ^2=7.8, φ=0.41, p < 0.006; OR=15.0 (1.6–142.0); DC_+=+5, DC_=–6.

2. **Isthmic-cervical insufficiency**: yes or no.

χ^2=7,6, φ=0.40, p < 0.006; OR=9.6 (1.7–55.0); DC_+=+5, DC_=–5.

3. **Newborn's birth weight**: <2,500 g or >3,500 g or ⩾2,500 g.

χ^2=8.4, φ=0.41, p < 0.004; OR=8.9 (1.7–45.0); DC_+=+5, DC_=–3.

4. **CA-125 level**: ⩾30 IU/mL or <30 IU/mL.

χ^2=9,7, φ=0,43, p < 0.002; OR=7.0 (1.7–31.0); DC_+=+6, DC_=–3.

5. **Myopia**: yes or no.

χ^2=5.6, φ=0.32, p < 0.02; OR=4.5 (1.2–20.0); DC_+=+5, DC_=–2.

Table 2. Prognostic table for identifying the risk of secondary ovarian masses in pregnant women

Risk factors	Gynecological history	Medical history data of the current pregnancy	Laboratory data	Somatic pathology	Medical history data of the newborn
Abortion before the second childbirth					
Yes	+5	–	–	–	–
No	–6	–	–	–	–
Initiation of sexual activity before 18 years old					
Yes	+3	–	–	–	–
No	-4	–	–	–	–
Isthmic-cervical insufficiency					
Yes	-	+5	–	–	–
No	-	–5	–	–	–
CA-125 level ⩾30 IU/mL					
Yes	–	–	+6	–	–
No	–	–	–3	–	–
Anemia					
Yes	–	–	+3	–	–
No	–	–	–3	–	–
Myopia					
Yes	–	–	–	+5	–
No	–	–	–	–2	–
Newborn's birth weight					
More than 2500 g and less than 3500 g	–	–	–	–	+5
From 2500 to 3500 g	–	–	–	–	–3

6. **Initiation of sexual activity**: under the age of 18 or after the age of 18.

χ^2=5.2, φ=0.31, p < 0.0001; OR=4.3 (1.1–16.0); DC_+=+3, DC_- =–4.

7. **Anemia**: yes or no.

χ^2=4.0, φ=0.30, p < 0.05; OR=3.3 (1.1–11.0); DC_+=+3, DC_-=–3.

Since this study was aimed to test the ability to predict recurrence of ovarian masses, the decision thresholds were rounded to +10 and –13. According to published studies, the recurrence rate of this ovarian pathology is approximately 14% and varies between 10%–20% [6]. We used a compromise estimate of 15% with an a priori DC of –8.

Moreover, this prognostic table was applied to a random sample of 24 pregnant women with ovarian masses removed either in the second trimester or during cesarean delivery. The algebraic sum of all DCs was <–13 in 15 women and >–13, but <+10 in nine women. Medical history analysis showed that all these women had no recurrence of ovarian masses at follow-up. Consequently, the predictive accuracy in the new sample was 62%.

DISCUSSION

The analysis of risk factors included in the diagnostic models shows that ovarian masses are a pathology, the development of which is influenced by somatic and gynecological diseases, menstrual disorders, and others [13]. A variety of factors were identified as contributing to the disruption of neuroendocrine regulation of hypothalamic function, including childbirth, abortion, infection, stress, surgery, and trauma. This disruption involves multiple systems, including the hypothalamic-pituitary-adrenal axis, the hypothalamic-pituitary-ovarian axis, and the autocrine and endocrine systems of visceral adipose tissue [14]. According to the World Health Organization, obesity has reached epidemic proportions in the 21st century. Projections indicate that by 2025, 40% of men and 50% of women will be affected by this condition [15]. Conversely, obesity results in menstrual cycle disorders, as evidenced by the analysis of Raikova et al. [16]. The analysis conducted by Nesterenko et al. [17] is of particular interest. It found that 20% of pregnancy terminations in women were complicated by ovarian cysts. The present study showed that the number of pregnancies and abortions, which became

one of the risk factors for ovarian masses, was lower in the main group than in the control group, although abortion itself is a risk factor [17]. This paradox may be attributed to the numerous obstacles to pregnancy in group 1. These include diseases and pathologies of the reproductive system, as well as organizational, environmental, and technological components. Additionally, social status and material opportunities of the individual [18] were not taken into account in the present study. Endometriosis is the most prevalent form of ovarian masses and the most common form of genital endometriosis, contributing to the development of endometriomas [19, 20]. According to the PLCO (Prostate, Lung, Colorectal and Ovarian Cancer) trial, the determination of the protein marker CA-125 in the blood is important in the screening of ovarian masses [21]. The level of this marker is influenced by increased body mass index [22], uterine fibroids, endometriosis, and pregnancy, which may lead to difficulties in interpretation [23] and its use during pregnancy [24]. However, there is evidence that the serologic level of CA-125 in the first trimester of pregnancy (up to 10 weeks) reaches a level of 1250 ME/mL and then decreases to 35 ME/mL by delivery [25, 26]. In addition, the created diagnostic rule indicates that high CA-125 levels in the second and third trimesters should be considered. Extragenital diseases, such as anemia, are a very important factor in the development of fetoplacental growth failure [27]. According to the published data, the incidence of fetoplacental insufficiency in pregnancies with ovarian masses ranges from 40%–45% to 100% [28], which may result in low-birth-weight babies. According to studies [29–31], the risk of miscarriage ranges from 43.9% to 77.8% of all cases and most often manifests as isthmic-cervical insufficiency. The occurrence of the phenomenon is associated with a defect in the cervix [32]. Common causes of isthmic-cervical insufficiency include rupture during childbirth, medical abortion, repeated cervical canal dilation, conization, trachelectomy [33–35], and inflammatory and/or infectious processes [36] that occur as a result of sexual debut before the age of 18, abortions, and a history of frequent changes in sexual partners [35, 37, 38]. The presence of undifferentiated forms of connective tissue dysplasia is a predictor of isthmic-cervical insufficiency [39] and myopia [40–44]. In myopia, scleral thickness, elasticity, and strength parameters are reduced due to low glycosaminoglycan content, total collagen, and weakening of the cross-links that stabilize the collagen fiber [45, 46]. Consequently, women with a history of the above factors may be classified as a risk group for the development of ovarian masses during pregnancy.

CONCLUSION

The study findings demonstrated that a rule predicting occurrence of primary and secondary ovarian masses based solely on clinical, anamnestic, and laboratory data may be created. The correlation between the prognostic assessment and the actual state of the patient was found to be satisfactory, particularly in cases involving primary masses. This rule requires further correction on larger samples and the introduction of additional indicators that could be regarded as risk factors in the analysis to achieve more reliable and stable prognoses. This may be important for rational treatment and management of such patients, even prior to ultrasound or surgical intervention. However, given the above probabilities of primary tumorigenesis and subsequent secondary tumorigenesis, the probability of unintentionally finding a pregnant woman with recurrent pathology in a random sample is only 0.5% to 1.0%. This combination, therefore, is a rare event. Consequently, obtaining a sufficient sample size for such pathologies is often time-consuming.

ADDITIONAL INFORMATION

Authors' contribution. D.A. Fatkullina: literature review, collection and analysis of literary sources, preparation and writing of the text of the article; A.G. Yashchuk: curation, surgical treatment of the patient, collection and analysis of literary sources, preparation and writing of the text of the article; I.I. Musin: surgical treatment of the patient, literature review, collection and analysis of literary sources, writing the text and editing the article; E.M. Gareev: literature review, collection and analysis of literary sources, writing the text and editing the article. All authors confirm that their authorship meets the international ICMJE criteria (all authors have made a significant contribution to the development of the concept, research and preparation of the article, read and approved the final version before publication).

Ethics approval. The study was conducted as part of D.A. Fatkullina's dissertation research and was approved by the Local Ethics Committee of Bashkir State Medical University, Ministry of Health of the Russian Federation (Protocol No. 9 dated November 17, 2021).

Consent for publication. Written consent was obtained from all the study participants before the study screening in according to the study protocol approved by the local ethic committee.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Д.А. Фаткуллина — обзор литературы, сбор и анализ литературных источников, подготовка и написание текста статьи; А.Г. Ящук — курация, хирургическое лечение пациента, сбор и анализ литературных источников, подготовка и написание текста статьи; И.И. Мусин — хирургическое лечение пациента, обзор литературы, сбор и анализ литературных источников, написание текста и редактирование статьи; Е.М. Гареев — обзор литературы, сбор и анализ литературных источников, написание текста и редактирование статьи. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

Этическая экспертиза. Исследование выполнялось в рамках диссертационной работы Д.А. Фатуллиной и его проведение согласовано с локальным этическим комитетом ФГБОУ ВО «Башкирский государственный медицинский университет» Министерства здравоохранения Российской Федерации (протокол № 9 от 17.11.2021 г.).

Согласие на публикацию. Все участники до включения в исследование добровольно подписали форму информированного согласия, утверждённую в составе протокола исследования этическим комитетом.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Раскрытие интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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