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RISK FACTORS FOR THE DEVELOPMENT, PREDICTION AND PREVENTION OF GESTATIONAL AND PERINATAL COMPLICATIONS DUE TO ADENOMYOSIS

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Abstract
Department of Obstetrics and Gynecology Tashkent Medical Academy Annotation Achieving favorable gestational and perinatal outcomes in women with adenomyosis is extremely important. The purpose of the study was to determine the pathogenetic role of adenomyosis in the development of obstetric and perinatal complications to improve the method of treating pathology with pre-conception preparation and to develop a prediction method complication during gestation.

Keywords: Adenomyosis, complications of pregnancy and childbirth, prevention of pregnancy complications Relevance. In the Republic of Uzbekistan, as in other countries of the world, issues of maternal and child health are one of the priority areas of modern medicine [2,5]. Today, women's reproductive health is considered as the most important general medical and social problem, which is the focus of constant attention of the world's leading scientific centers.

Introduction

Based on numerous studies, a number of factors have been established that increase the risk of developing a pathological course of pregnancy. Among them, a special role is given to adenomyosis, a pathology that leads to disruption of the processes of implantation and placentation.

An important area of research is the analysis and determination of the degree of participation of various forms of adenomyosis in the development of obstetric and perinatal complications, search for markers for preclinical prediction of gestational complications and development of methods for preventing predicted pathologies. The purpose of the study was to determine the pathogenetic role of adenomyosis in the development of obstetric and perinatal complications in order to improve the method of treating pathology with prenatal preparation and to develop a method for predicting complications during gestation

Materials and Methods

To achieve this goal, we identified tasks, one of which was to analyze the frequency and structure of obstetric and perinatal complications in women with AM. Materials and methods of research. The study was carried out in several stages. At the first stage, in order to determine the frequency and structure of obstetric and perinatal complications in 103 women with various forms of adenomyosis aged 25 to 35 years (average age 29.6±4.2 years),. who received

outpatient treatment in the department of polyclinic 9 of the obstetric complex and the private clinic NS Medical in Tashkent for the period from 2021-2023, a comparative prospective study was carried out with the study of clinical and anamnestic data of the study, depending on the form of pathology. Depending on the form of adenomyosis, women were divided into groups: Group 1 consisted of 82 women with a diffuse form of adenomyosis, of which 69 women had grade 1-2 AM and 13 women had grade 3 AM; Group 2 - 21 women with focal form of adenomyosis. The control group included 112 women without adenomyosis in the same age range. At this stage, the effectiveness of previously received therapy for adenomyosis was also assessed and an improved method of treating adenomyosis was proposed, including epigenetic therapy.

At the second stage of the study after treatment for adenomyosis, pregnancy planning was carried out. When pregnancy occurred in 66 (64.1%) women studied, the level of trophoblastic glycoprotein was determined in pregnant women with adenomyosis during gestation, with various obstetric and perinatal complications, and its prognostic significance was determined.

Depending on management, pregnant women were divided into subgroups. 1 subgroup consisted of women (n=45), of which 34 women had a diffuse form of AM and 11 with a focal form, who were prescribed micronized progesterone at a dose of 400 mg per day until the 16th week of pregnancy and acetylsalicylic acid 75 mg per day to prevent gestational complications. day from 12 to 36 weeks of pregnancy. Subgroup 2 consisted of pregnant women (n=21), of which 13 women had a diffuse form of AM and 8 with focal AM, who were managed traditionally. The comparison group consisted of 42 pregnant women without adenomyosis.

Results and Discussion

It is noted that adenomyosis occupies an important place among the risk factors for the development of obstetric and perinatal complications, namely spontaneous miscarriages, NB, premature birth, perinatal losses and pathology, complications of childbirth and the postpartum period. Adenomyosis plays a special role in the formation of very early and early PR. A large group consists of women with the development of destructive processes in the placenta, clinically manifested as PD. ORP, hypertensive disorders, PR. All these complications of gestation in the history of women with adenomyosis, identified in our studies, are consistent with the literature data [5, 9, 13] and served to distribute them according to the degree of influence of adenomyosis in the formation of obstetric and perinatal complications and determine the timing of the examination.

In the history of women with adenomyosis, the most common gestational complications were spontaneous miscarriages (23.3%), placental dysfunction (31.1%), hypertensive disorders (27.2%), premature birth (24.3%), placenta previa (7.8%), perinatal losses (29.1%), (29.1%), as well as postpartum hemorrhage (12.6%), uterine subinvolution (24.3%).

To identify the cause-and-effect relationship between adenomyosis and the development of gestational complications, we calculated the chance (OR) and risk (RR) of the occurrence of gestational complications in these patients. From the point of view of evidence-based medicine, the chances and relative risk of developing obstetric and perinatal complications are high in women with adenomyosis, the structure of which is: very early and early preterm birth

(OR=17.5; RR=15.6), spontaneous miscarriages (OR=2.8; RR=2.4), placental dysfunction (OR=2.9; RR=2.4), hypertensive disorders (OR=3.1; RR=2.5); preterm birth (OR=2.6; RR=2.2), ORP (OR=5.7; RR=5.6), presentation (OR=3.1; RR=2.7) and abnormal placenta attachment (OR=4.0; RR=3.5), as well as bleeding in the postpartum period (OR=2.2; RR=2.1) and uterine subinvolution (OR=2.4; RR=2.0).

Thus, women with adenomyosis are characterized by a high frequency of reproductive losses, complications of gestation, childbirth and the postpartum period, which necessitates the identification and timely treatment of this pathology with the prevention of its relapses in combination with pre-conception preparation, as well as the search for markers for predicting obstetric and perinatal complications of gestation and methods of their prevention. Исследования зарубежных авторов показали взаимосвязь большего количества гестационных осложнений с отсутствием полного нивелирования очагов аденомиоза, а также развитием рецидива патологии после терапии [6, 8]. В связи с этим нами были изучены методы и длительность терапии аденомиоза, ее эффективность, побочные эффекты и осложнения.

Of the 103 women with a history of adenomyosis, slightly more than half of the women received therapy for the pathology (n=71, 68.9%), the remaining 32 (31.1%) women did not receive therapy for adenomyosis due to an unidentified diagnosis. These women, when visiting a gynecologist and presenting with complaints characteristic of adenomyosis, were more often mistakenly diagnosed with chronic endometritis, NMC, and less often with uterine fibroids (in the focal form of AM).Accordingly, subsequent therapy was not effective and high reproductive losses were observed when pregnancy occurred (55.3%).

A study of treatment methods for adenomyosis in 71 women showed that only 19 (26.8%) women received GnrH agonists (mainly diferelin, zoladex and decapeptyl). Their duration of therapy averaged 4.6±1.4 months. Apparently, this was due to grade 1-2 severity of adenomyosis, or the high cost of the drugs did not allow them to be widely used in clinical practice. A survey of women taking GnrH agonists showed a high incidence of side effects - in 17 (89.5%) out of 19 women.

remaining 52 women with adenomyosis received drugs containing dienogest at a dose of 2 mg/day in a continuous mode (Visanne, Zafrilla). The duration of therapy also varied and averaged 4.5±2.5 months. When using dienogest, the incidence of side effects was significantly lower (36.6%) and milder than in women using GnRH agonists. While taking dienogest, pregnancy occurred in more than a quarter (26.7%) of women before the end of therapy Apparently, further unfavorable course of pregnancy is associated with incomplete leveling of foci of adenomyosis. The recurrence rate of adenomyosis with this therapy was 23.1%.

Considering the high rate of relapse of adenomyosis after therapy (32.4%), we decided to improve the method of administration for women with this pathology.At stage I, therapy for adenomyosis should be carried out with dienogest-containing COCs (Zhanin, dieenogest 2 mg/day) for 6 months (for greater leveling of lesions and contraception), and also include a drug that affects another epigenetic link of pathogenesis, Indole-3-carbinol (I3C) in continuous regimen (200 mg/day) for a year/before pregnancy. Indole-3-carbinol (I3C) is a dietary supplement of natural origin that has specific epigenetic activity, the mechanism of action of

which in AM is to stabilize the genome by inhibiting DNA methylation and suppressing DNA methyltransferase, which helps suppress the processes of estrogen-dependent and estrogen-independent proliferation and neoangiogenesis, suppression of inflammation, stimulation of apoptosis.

The severity of pain syndrome according to VAS before the start of therapy was assessed by 79.6% of those examined in the main group at 6.6±0.8 points, while in the group of women without adenomyosis it was 2.8±1.6 points ($p<0.001$). Regression of pelvic pain by the end of therapy was noted by 61.9% of women with a diffuse form of AM (from 7.4 points to 3.3 points) and 76.2% of participants with a focal form of AM (from 6.3 points to complete relief).

The study of blood circulation indicators in the vessels of the uterus in dynamics during complex therapy showed that in women with a diffuse form of AM in 28.6% of cases and in women with focal AM in 47.6%, normalization of blood flow indicators was revealed, which apparently subsequently influenced the successful outcome of pregnancy.

The next stage of the study was planning pregnancy and studying its course, depending on the management method. In order to prevent relapse of AM after the end of therapy with dienogest-containing COCs, we continued therapy with indole-3-carbinol in a continuous mode (200 mg/day) for another 6 months, or until pregnancy (if it occurred earlier). The complicated course of gestation in women with AM, often miscarriage, prompted us to provide progesterone support during pregnancy. To prevent miscarriage, we prescribed micronized progesterone at a dose of 400 mg per day until the 16th week of pregnancy and acetylsalicylic acid 75 mg per day from 12 to 36 weeks of pregnancy.

Within a year after the end of therapy, out of 103 women with AM, 66 (64.1%) women became pregnant, while in the diffuse form of adenomyosis, pregnancy occurred in 47 of 82 women (57.3%), which is 1.6 times less likely than with focal AM (90.5%) (19 out of 21). Depending on the management, 66 pregnant women with AM were divided into groups. The group consisted of 37 women who received prevention of complications. Group B consisted of 21 women who did not receive complications prevention,of these, 21 were with the diffuse form and 8 were with the focal form of AM.

An analysis of the course and outcomes of pregnancy in women with AM showed that women who received prophylaxis had a more favorable course of pregnancy with fewer complications. Thus, the threat of miscarriage was observed in more than half of women (65.5%) with traditional management, while in pregnant women managed comprehensively - in 35.1%.Similarly, lower rates of PD (18.9%), SORP (6.9%), very early and early PR (5.4%), PE (13.5%) were noted in the group with complex management.

The comprehensive management of women with AM also affected the course of labor. In 13.8% of women in labor with AM, during traditional management, labor was weak, which is almost 2 times more often than in the group receiving indole-3-carbinol and prevention of gestational complications. The rate of cesarean section in pregnant women with traditionally managed AM was higher than population indicators and amounted to 27.6%. A relatively low (21.6%) proportion of cesarean sections, not different from the population frequency, in the group of pregnant women managed comprehensively,indicates a satisfactory condition of the pregnant woman and the intrauterine fetus.

Analysis of pregnancy outcomes in groups of patients showed that the average duration of pregnancy and the frequency of timely births were significantly higher in the group of women with adenomyosis who received indole-3 carbinol before pregnancy, and micronized progesterone and acetylsalicylic acid during gestation ($\chi 2=6.37$; $P<0.05$), while the incidence of preterm birth was significantly lower by 1.5 times ($\chi 2=3.52$; $P<0.02$), and the frequency of fetal loss is more than 1.5 times ($\chi 2=3.69$; $P<0.05$).

The favorable course of pregnancy with comprehensive management of AM also affected the condition of the newborn.Anthropometric indicators of newborns whose mothers were managed comprehensively were similar to those of controls, while in pregnant women with AM without prevention they were lower. As a result of comprehensive management of pregnant women with AM, the number of healthy newborns has increased more than 3 times, and their morbidity rate has decreased by 2 times.

Considering all of the above, it becomes clear the advantage of an integrated approach to the management of pregnant women with adenomyosis, based on treatment with the prevention of relapses (indole-3 carbinol) and gestational complications (micronized progesterone and acetylsalicylic acid).

The study of the functionality of the placenta, the main element in the mother-fetus system, has acquired key importance in the field of obstetrics. Among the pathomorphological signs in the placenta of women with AM, there are clearly interconnected processes leading to the destruction of the placenta. Characteristic changes in placentas during the development of pregnancy complications against the background of adenomyosis were placental hypoplasia, acute and chronic circulatory disorders, dystrophic and ischemic processes. This was manifested by a decrease in the number of blood vessels in the stem and terminal villi, fibrinoid degeneration of the villous epithelium, deposition of fibrinoid on the side of the intervillous space, reduction in the volume of the intervillous space, infarction, enlargement of symplastic kidneys with signs of dystrophy, as well as dominance of intermediate villi. The severity of these changes differed in placental biopsies from women with various pregnancy complications.

We also identified correlations between the histomorphological parameters of the placenta and obstetric complications (preeclampsia, PD, PR and ORP), which indicate similar mechanisms for the development of the studied complications of gestation in adenomyosis.

To determine the relationship between the development of gestational complications and the level of trophoblastic β-1-glycoprotein in pregnant women, We conducted studies of this marker in blood serum over the dynamics of gestation. Depending on the type of obstetric and perinatal complications and gestational age, different serum levels of trophoblastic β-1-glycoprotein were noted.At the same time, in the sequence of dynamics of decrease in trophoblastic β-1-glycoprotein in the blood serum of pregnant women with various complications, the severity of the indicators was distributed in the following order: I place was taken by spontaneous miscarriages and placental dysfunction, II place by ORP and PE, III by very early and early premature birth.This, in turn, will make it possible, based on studying the level of TBG, to predict obstetric complications in women with adenomyosis at the preclinical stage. When the values of trophoblastic β-1-glycoprotein are below standard values at the

appropriate time (up to 12 weeks less than 16,500±15.9 ng/ml, 13-22 weeks - 29,518.6±12.5 ng/ml, 23-27 weeks –58,597.2±13.9 ng/ml, 28-34 weeks – 232,635.8±11.3ng/ml),the risk of spontaneous miscarriage and placental dysfunction is predicted to be 2 times higher; 2.3 times – preeclampsia and ORP; 3.6 times - preterm birth and 5.3 times - development of very early and early preterm birth ($p < 0.001$).

It should also be noted that by changing the level of trophoblastic β-1-glycoprotein in patients with threatened preterm birth, one can judge the effectiveness of the ongoing conservation therapy, which is confirmed by correlation analysis data ($r = 0.85$, $p = 0.019$).

The proposed method gives the probability of a correct prognosis in the 2nd trimester - 90%, in the third trimester - up to 95.5% of cases. With a high degree of probability, it is possible to predict the outcome of pregnancy depending on the level of trophoblastic β-1-glycoprotein, which makes it possible to determine pregnancy management tactics.

Conclusion

Summarizing the results of the study, we can conclude that the most characteristic complications of pregnancy in AM are PD, very early and early preterm birth, PE, ORP and relatively low birth weight of children. Carrying out comprehensive management with improvement of AM therapy including epigenetic therapy, with the prediction and prevention of gestational complications made it possible to significantly reduce the pathological course of pregnancy and childbirth, and also reduce perinatal morbidity and mortality.

REFERENCES.

1.Adamyan L.V., Serov V.N., Sukhikh G.T., Fillipov O.S. Clinical recommendations. Obstetrics and gynecology. Endometriosis: diagnosis, treatment and rehabilitation. // Problems of reproduction. - 2017. No. 6. - P.553-605.

2.Zayratiants O.V., Andreeva E.N., Adamyan L.V., Sonova M.M., Urumova L.T., et al. Endometriosis: new experience of non-hormonal drug therapy. // Problems of reproduction. - 2018. No. 24(6). P.113-120. https://doi.org/10.17116/repro201824061113.

3.Kutsenko I.I., Kravtsova E.I., Avakimyan V.A., Tomina O.V., Storozhuk P.G. Hormone-mediated cytokine regulation of endometrial implantation potential in patients with adenomyosis with unsuccessful IVF attempts // Kuban Scientific Medical Bulletin. – 2017.-№4.-P.91-95.

4.Mogilnaya G.M., Kutsenko I.I., Simovonik A.N. Morphometric characteristics of cell nuclei in the myometrial transition zone in adenomyosis. // Kuban Scientific Medical Bulletin. - 2016. - No. 3. – P.88-91. https://doi.org/10.25207/1608-6228-2016-3-88-91.

5.Saidzhalilova D.D., Madolimova N.Kh. Complications of pregnancy and childbirth in patients with endometriosis // XVI International Congress on Reproductive Medicine, 2023, 191-192

6.Berlac J.F., Hartwell D., Skovlund C.W., Langhoff-Roos J., Lidegaard Q. Endometriosis increases the risk of obstetrical and neonatal complications. // Act.Obstet.Gynecol.Scand. 2017.Vol.96(6).P.751-760. https://dx.doi.org/10.1111/aogs.13111

7.Brown J., Crawford T.J., Allen C. et al. Nonsteroidal anti-inflammatory drags for pain in women with endometriosis. // Cochrane database Syst. Rev. – 2017/ - Vol. 1. – P.CD004753.
8.Hamdan M., Omar S.Z., Dunselman G., Cheong Y. Influence of endometriosis on assisted reproductive technology outcomes: a systematic review and meta-analysis // Obstet. Gynecol. - 2015. - Vol. 125. № 1. - P. 79-88. https://dx.doi.org/10.1097/AOG.0000000000000592
9.Carrarelli P., Yen C.F., Funghi L. et al. Expression of Inflammatoryand Neurogenic Mediators in Adenomyosis: A Pathogenetic Role.// Reprod.Sci. 2017; 24: 369–375.
10.Casper R.F. Progestin-only pills may be a better first-line treatment for endometriosisthan combined estrogen-progestin contraceptive pills // Fertill. Steril. -2017. – Vol. 107, №3.-P. 533-536.
11.Leyendecker G., Kunz G., Kissler S., Wildt L. Adenomyosis andreproduction. // Best Practice & Research Clinical Obstetrics &Gynaecology. 2016; 20: 523–546.
12.Petraglia F, Arcuri F, de Ziegler D, Chapron C. Inflammation: alink between endometriosis and preterm birth. // Fertil.Steril. 2018;98.
13.Saidjalilova D.D., Madolimova N.Kh., Ayupova D.A. Influence of endometriosis in course of pregnancy and childbirth// Tibbiyotda yangi kun, 8(46),2022, 74-78.
14.Vercellini P, Consonni D, Dridi D, Bracco B, FrattaruoloMP,Somigliana E. Uterine adenomyosis and in vitro fertilizationoutcome: a systematic review and meta-analysis. // Hum.Reprod.2014; 29: 964–977.