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Pregnancy and labor in patients with uterine fibroids

Yulia E. Dobrokhotova[1], Aznar S. Khachatryan[2], Irina Yu. Ilyina[1], Djamilia M. Ibragimova[1], Metanat R. Narimanova[1], Elena S. Platova[1], Olga I. Kauseva[3]

[1] Pirogov Russian National Research Medical University, Moscow, Russia;
[2] Yerevan State Medical University, Yerevan, Armenia;
[3] City Clinical Hospital No. 1 named after N.I. Pirogov, Moscow, Russia

ABSTRACT

This review examines the etiology, pathogenesis, clinical manifestations, and impact of uterine fibroids on reproductive function. Particular attention is given to infertility, pregnancy, and labor in patients with fibroids. Uterine fibroids may be asymptomatic or present with various symptoms, including menstrual irregularities and pelvic pain. The review discusses the effect of fibroids on conception, fetal development, and the risk of pregnancy and labor complications. The influence of fibroids on pregnancy outcomes is determined by their location, size, and number. With the increasing maternal age of women planning pregnancy, the prevalence of uterine fibroids in this population is also rising. As a result, organ-preserving surgical approaches aimed at optimizing reproductive outcomes and reducing pregnancy complications have become a primary treatment strategy. However, the best management strategy that minimizes complications and alleviates symptoms remains undefined. Treatment decisions should be individualized, taking into account multiple factors and requiring thorough patient evaluation. The review underscores the importance of early detection and prevention of pregnancy-related complications in patients with uterine fibroids. Further research is essential to refine preventive measures and optimize treatment strategies for this condition.

Keywords: uterine fibroids; myomectomy; recurrent pregnancy loss; preterm birth; uterine rupture; pregnancy complications.

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Течение беременности и родов у пациенток с миомой матки

Ю.Э. Доброхотова[1], А.С. Хачатрян[2], И.Ю. Ильина[1], Д.М. Ибрагимова[1], М.Р. Нариманова[1], Е.С. Платова[1], О.И. Каусева[3]

[1] Российский национальный исследовательский медицинский университет им. Н.И. Пирогова, Москва, Россия;
[2] Ереванский государственный медицинский университет, Ереван, Армения;
[3] Городская клиническая больница № 1 им. Н.И. Пирогова, Москва, Россия

АННОТАЦИЯ

В представленном обзоре обсуждаются вопросы этиологии, патогенеза, клинических проявлений и влияния миомы матки на репродуктивную функцию женщины. Особое внимание уделяется проблемам бесплодия, беременности и родов при наличии миомы. Отмечается, что данное заболевание может протекать бессимптомно или сопровождаться различными жалобами, такими как нарушения менструального цикла, болевой синдром и другие. Также обсуждается влияние миомы матки на возможность забеременеть, на развитие плода, на частоту осложнений беременности и родов. Влияние миомы матки на наступление и течение беременности определяется локализацией, размерами и количеством узлов. В настоящее время возраст женщин, планирующих беременность, постепенно растёт, в связи с чем увеличивается вероятность наличия у них миомы матки. Поэтому основным хирургическим направлением являются органосохраняющие операции с целью подготовки пациенток к беременности и уменьшения рисков развития осложнений. Какое именно лечение может привести к оптимальному результату, наименьшему количеству осложнений, уменьшению симптомов, на сегодняшний день окончательно не установлено, это зависит от многих факторов и требует тщательного отбора и обследования пациенток. В заключение обзора подчёркивается важность раннего выявления и предотвращения осложнений беременности при миоме матки, отмечается, что дальнейшие исследования в этой области могут помочь в разработке эффективных методов профилактики и лечения данного заболевания.

Ключевые слова: миома матки; миомэктомия; невынашивание беременности; преждевременные роды; разрыв матки; осложнения беременности.

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子宫肌瘤患者的妊娠及分娩过程

Yulia E. Dobrokhotova[1], Aznar S. Khachatryan[2], Irina Yu. Ilyina[1], Djamilia M. Ibragimova[1], Metanat R. Narimanova[1], Elena S. Platova[1], Olga I. Kauseva[3]

[1] Pirogov Russian National Research Medical University, Moscow, Russia;
[2] Yerevan State Medical University, Yerevan, Armenia;
[3] City Clinical Hospital No. 1 named after N.I. Pirogov, Moscow, Russia

摘要

本综述探讨了子宫肌瘤的病因、发病机制、临床表现及其对女性生殖功能的影响，重点关注该疾病对不孕、妊娠及分娩的影响。研究表明，子宫肌瘤可能为无症状，也可能伴随月经紊乱、疼痛综合征等各种临床表现。此外，本文还讨论了子宫肌瘤对受孕能力、胎儿发育以及妊娠和分娩并发症发生率的影响。子宫肌瘤对妊娠的发生及进展的影响取决于其位置、大小及数量。近年来，计划妊娠的女性年龄逐渐上升，因此，子宫肌瘤的患病率也相应增加。因此，当前的手术策略主要以保留子宫的方式进行，以帮助患者备孕并降低妊娠并发症的风险。然而，目前尚未明确哪种治疗方案最优，可最大程度减少并发症并改善症状。治疗选择受多种因素影响，需要对患者进行详细筛查和个体化评估。本综述最后强调了早期发现子宫肌瘤及预防妊娠并发症的重要性，并指出该领域的进一步研究可能有助于开发更有效的预防和治疗策略。

关键词：子宫肌瘤；子宫肌瘤切除术；流产；早产；子宫破裂；妊娠并发症。

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INTRODUCTION

Uterine fibroids (UFs) are defined as benign, dyshormonal, and capsulated neoplasms that develop from smooth muscle cells. Together with fibroblasts, these cells comprise the myomatous nodule [1–4].

Pregnancy in UFs has been documented in 0.5% to 6.0% of cases [5, 6]. However, the current data on the UF incidence in pregnant women is controversial. Firstly, there is an observed trend toward an increased incidence of UFs in pregnancy, attributable to women who more frequently postpone childbearing to a later age. Secondly, there is an observed increase in the UF incidence among women under 30 years of age who have not yet undergone childbearing [7, 8].

ETIOLOGY AND PATHOGENESIS OF UTERINE FIBROIDS

The UF growth depends on hormonal changes in the female body, with estrogens and progesterone traditionally considered to be the stimulators of fibroid growth [8–11].

In addition, growth factors play a major role in fibroid development. These include insulin-like growth factors, vascular endothelial growth factor, hypoxia-inducible factor, fibroblast growth factor, platelet-derived growth factor, angiogenin, epidermal growth factor, nitric oxide, interleukin-8, and matrix metalloproteinases. Chromosomal rearrangements associated with increased expression of the *HMGA2* gene and somatic gene mutations in exon 2 of the *MED12* gene encoding RNA polymerase 2 contribute significantly to the pathogenesis of UFs. All of these factors form a complex system of interactions involved in the molecular pathogenesis of this condition [8, 12–14].

Furthermore, the process of neoangiogenesis, defined as the formation of new blood vessels from existing ones, has been identified as a pivotal factor in the development of UFs [8]. Additionally, there is an opinion that oxidative stress may contribute to fibroid formation, impacting platelet aggregation and activating the coagulation cascade. This, in turn, results in impaired endothelium-dependent vasodilation and stimulation of smooth muscle cell proliferation, which, consequently, leads to the development of primary fibroids [15–17].

Despite the many known factors involved in the development of UFs, there is no complete understanding of the exact pathogenesis of this disease. Clarification of the causative factors could facilitate the implementation of preventive measures and effective treatment strategies for UFs.

CLINICAL PRESENTATION OF UTERINE FIBROIDS

Approximately 77% of women exhibit asymptomatic UF, which are often detected occasionally during examination. However, 15%–30% of patients may experience symptoms, including menstrual dysfunction, pain syndrome, infertility, and recurrent pregnancy loss [8, 18–20], which may seriously affect their quality of life and reproductive potential [6, 7, 11, 17, 18, 21].

UTERINE FIBROIDS AND FEMALE FERTILITY

The role of UFs in the development of infertility remains a subject of debate. The mechanisms by which this condition may lead to reproductive dysfunction remain unclear [22].

Obviously, the effect of fibroids on pregnancy is determined by their localization, size, and number [7, 23, 24].

According to some authors, the frequency of UF in infertility is 25%–27% [25, 26]. It is suggested that UF may lead to infertility in only 2%–3% of cases.

Undoubtedly, submucosal UF has a greater impact on the possibility of pregnancy, since this category of patients has a lower implantation rate, an increased rate of spontaneous abortion, more often develops placental insufficiency and pregnancy complications associated with abnormal localization of the placenta or its premature abruption [7, 8, 27]. Consequently, the incidence of pregnancy and implantation is lower in patients with submucosal UFs compared with infertile patients. The removal of submucosal fibroids improves fertility.

In some cases, UF does not prevent pregnancy and fetal development; however, it may increase the likelihood of adverse pregnancy and labor outcomes [8, 26, 28].

As previously mentioned, the incidence of UF in pregnancy is not uncommon in the contemporary world, whereas the frequency of complications is high. This combination poses a significant risk for potential complications. Early detection and prevention of these complications are crucial to reduce maternal and fetal morbidity [8, 15, 29, 30].

For instance, the study demonstrated that pregnancy in women with UF frequently occurs concomitantly with anemia grade I and II, accounting for up to 84.5% of cases. This trend has been observed in pregnant women with multiple UFs [30].

In the presence of UF, one of the complications is recurrent pregnancy loss, which may develop as a result of impaired blood supply and endometrial receptivity, preventing normal implantation of the embryo and disrupting placental development. As stated above, hyperhomocysteinemia has been identified as a potential contributing factor to the development of UF. In women with elevated homocysteine levels, endothelial cell activation is altered during pregnancy, leading to an increased risk of thrombosis. During chorionic development, initial damage to the vascular endothelium may lead to dysfunction of the fetoplacental complex, resulting in miscarriage or placental insufficiency [15, 16].

The coexistence of pregnancy and UF is associated with an increased prevalence of intramural nodal localization

(68%). A possible complication may be a nutritional disorder in the myomatous nodule, as well as an increased risk of preterm delivery, antenatal rupture of fetal membranes, and placenta previa in the third trimester of pregnancy. Postpartum hemorrhage is common in this group of patients. Numerous studies [7, 27, 30, 31] have demonstrated a favorable prognosis for the fetus.

In addition, the data demonstrate a direct proportionality between the percentage of women with full-term pregnancies delivered by cesarean section and the age of the pregnant woman. The findings reveal a statistically significant increase in the cesarean section rate, from 16.7% in the 20–24-year age group to 61.0% in the 40–44-year age group and 100.0% in the 45–46-year age group. This association may be indicative of UF and other comorbidities [7].

TREATMENT OPTIONS FOR UTERINE FIBROIDS

It is important to consider lifestyle modification, which may also contribute significantly to the development of UFs (obesity, lack of physical activity, and smoking) [32].

The majority of pharmacological agents approved for the treatment of UF have a therapeutic effect only during their use; after withdrawal, disease progression may occur. In addition, adverse effects associated with the use of these medications limit their widespread use [33].

Surgical treatment of UFs includes hysterectomy, myomectomy, uterine artery embolization, and magnetic resonance-guided focused ultrasound [8, 18, 28, 34, 35].

As the age of women planning pregnancy increases, there is a need for fertility-sparing surgery aimed at eliminating the pathological process and preserving the reproductive organ [19, 36–38].

Hysteroscopic myomectomy is indicated for submucosal UF, which increases the likelihood of spontaneous pregnancy [8, 39, 40].

Conversely, abdominal myomectomy is recommended for the treatment of symptomatic and subserosal UFs in patients of reproductive age and is the gold standard of treatment [17, 25, 28].

There have been numerous studies aimed at identifying the optimal approach to myomectomy based on a comparative analysis between laparoscopic myomectomy and laparotomic myomectomy.

Laparoscopic myomectomy has undergone significant advancements, rendering it a safe option for women of reproductive age who are planning a pregnancy. However, uterine rupture remains a concern, occurring in rare cases irrespective of fibroid characteristics. Further study is necessary to determine the risk group for this complication [25–28, 41]. Consequently, there is a tendency to recommend laparotomy as the preferred approach; however, laparoscopic myomectomy may increase the risk of uterine rupture compared with other approaches [41].

Therefore, recent technological advancements make myomectomy a relatively safe procedure, positioning it as a potential mechanism for reproductive potential enhancement [8, 25].

EFFECT OF MYOMECTOMY ON PREGNANCY AND LABOR

In recent years, the indications for laparoscopic myomectomy prior to pregnancy planning have been expanded to prevent complications. This is due to the high incidence of complications during pregnancy and labor in patients with UF [23, 42–44].

Myomectomy in patients of reproductive age is intended to preserve their reproductive potential. The procedure is associated with significant risks; however, studies have shown that this surgical option significantly increases pregnancy rates in women with UF-related infertility [22, 45]. The use of laparoscopic and hysteroresectoscopic approaches in myomectomy has been shown to reduce the traumatic nature of the procedure and thus contribute to an increase in the postoperative pregnancy rate [46].

It is hypothesized that the most common complication following myomectomy is the potential for pregnancy loss (23.8%), with pre-eclampsia identified in 9.5% of pregnant women, placenta previa documented in 2.4%, and placental insufficiency recorded in 1.2% [22, 46].

Furthermore, there is evidence that the rate of pregnancy loss decreases after myomectomy, although the total number of pregnancy losses is higher than in the general population [47, 48].

Pregnant women with a history of myomectomy should be considered a risk group for miscarriage, placental insufficiency, and pre-eclampsia. A particular emphasis should be placed on post-myomectomy patients with a history of infertility, as they have a statistically higher risk of secondary uterine inertia combined with limited use of induction methods [30].

Certain complications such as scar failure, risk of uterine rupture along the scar (6.7%), and pelvic adhesions (16.7%) may be associated with vaginal delivery in patients after myomectomy [49].

However, surgical delivery is indicated for medical reasons in 72.6% of cases following myomectomy using various approaches. Vaginal delivery is a viable option in 60% of women who have undergone myomectomy using a hysteroresectoscopic approach in the absence of contraindications [46].

There is evidence suggesting the possibility of uterine rupture at the end of pregnancy or uterine scar rupture during labor after myomectomy. According to foreign authors, the risk of uterine rupture after myomectomy ranges from 0.5% to 1.5% [50, 51]. It is generally accepted that uterine scarring after myomectomy is the second most common cause of uterine rupture after cesarean section [43, 52].

The same opinion is shared by other researchers. According to their data, the risk of uterine rupture in a subsequent pregnancy after myomectomy ranges from 0.7% to 1.0% [53]. A systematic review of the publications was performed, including all cohort studies with at least five reported pregnancy outcomes after myomectomy. In the included studies, the overall incidence of uterine rupture after myomectomy was found to be 0.93% (0.45%–1.92%; 7/756), of which 0.47% (0.13–1.70%; 2/426) occurred during vaginal delivery and 1.52% (0.65–3.51%; 5/330) occurred before labor [51]. The present systematic review showed that uterine rupture after previous myomectomy occurred mostly before 36 weeks and before labor [51].

There are data suggesting that 90.4% of women who undergo myomectomy deliver vaginally without the risk of uterine scar rupture or serious maternal and perinatal complications. The authors emphasize that the mode of delivery depends on whether the uterine cavity was opened during the myomectomy or not [51–53].

A retrospective cohort study was conducted to compare cesarean section outcomes in women who underwent myomectomy with those who underwent cesarean section without a history of prior myomectomy. The analysis revealed that prior myomectomy in women with a full-term singleton pregnancy who underwent elective cesarean section was associated with an increased risk of intraoperative blood transfusion compared with the control group. However, other authors have suggested that increased blood loss may be observed in patients with large UFs (⩾5 cm), and that myomectomy performed before pregnancy might reduce the risk of hemorrhage [53, 54].

Many experts point out that in patients with a history of myomectomy, surgical delivery is preferable. Indeed, surgical delivery may become the method of choice, with current data indicating that it is employed in 85% of cases involving this condition. Cesarean delivery in such patients may be associated with an increase in the volume of surgical intervention in the form of myomectomy by indication (58.8%), which may lead to pathological blood loss (2.5%) [49, 55].

According to other authors, vaginal delivery is preferable. In cesarean delivery, myomectomy is advisable if a myomatous nodule prevents extraction of the fetus [8, 56].

Therefore, thorough preoperative preparation and intraoperative prevention of massive obstetric hemorrhage are necessary when planning cesarean delivery in pregnant women with a history of UF or myomectomy [57].

CONCLUSION

Myomectomy as a stage of pre-gravid preparation should be performed adhering to the established principles, ensuring not only the initiation but also the successful culmination of pregnancy [43, 58]. Pregnancy in patients with UF or a history of myomectomy should be regarded as a high-risk condition, necessitating heightened surveillance and monitoring. The current state of research reveals a lack of consensus regarding the management of patients with UF and/or a history of myomectomy who are planning to become pregnant. Further studies are necessary to provide definitive recommendations and clearer guidelines for case-by-case management [48, 59, 60].

In light of the observed trend of postponed childbearing at a later age in recent years, which has resulted in an increase in the number of pregnant women with UF, as well as the high risk of maternal and perinatal loss, it is necessary to develop an algorithm for the examination and management of this category of women. The objective of this algorithm is to successfully prolong pregnancy and prevent the development of complications during pregnancy, labor, and the postpartum period [61, 62].

ADDITIONAL INFORMATION

Authors' contribution. Y.E. Dobrokhotova: study conception, manuscript review, and final approval; A.S. Khachatryan: data collection and analysis; I.Yu. Ilyina: study conception, manuscript drafting, review, and final approval; D.M. Ibragimova: data collection and analysis; M.R. Narimanova: data acquisition, analysis, and manuscript editing; E.S. Platova: data collection and analysis; O.I. Kauseva: data collection and analysis. All authors confirm that their authorship meets the international ICMJE criteria (all authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work).

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Вклад авторов. Ю.Э. Доброхотова — разработка концепции статьи, проверка и утверждение текста статьи; А.С. Хачатрян — сбор и анализ данных; И.Ю. Ильина — разработка концепции статьи, написание, проверка и утверждение текста статьи; Д.М. Ибрагимова — сбор и анализ данных; М.Р. Нариманова — получение и анализ фактических данных, редактирование текста статьи; Е.С. Платова — сбор и анализ данных; О.И. Каусева — сбор и анализ данных. 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).

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AUTHORS' INFO

***Metanat R. Narimanova,** MD, Cand. Sci. (Medicine), Assistant Professor;
address: 1/6 Ostrovityanova st, Moscow, Russia, 117513;
ORCID: 0000-0003-0677-2952;
eLibrary SPIN: 2723-5711;
e-mail: safarovametanat@yandex.ru

Yulia E. Dobrokhotova, MD, Dr. Sci. (Medicine), Professor;
ORCID: 0000-0002-7830-2290;
eLibrary SPIN: 2925-9948;
e-mail: pr.dobrohotova@mail.ru

Aznar S. Khachatryan, MD, Cand. Sci. (Medicine), Assistant Professor;
ORCID: 0009-0000-2767-8995;
eLibrary SPIN: 7707-5981;
e-mail: aznardoc@yahoo.com

Irina Yu. Ilyina, MD, Dr. Sci. (Medicine), Professor of the Department;
ORCID: 0000-0001-8155-8775;
eLibrary SPIN: 5753-4380;
e-mail: iliyina@mail.ru

Djamilia M. Ibragimova, MD, Cand. Sci. (Medicine), Assistant Professor;
ORCID: 0000-0002-8738-868X;
eLibrary SPIN: 7962-4941;
e-mail: dgam81@mail.ru

Elena S. Platova, MD, Cand. Sci. (Medicine), Assistant Professor;
ORCID: 0009-0009-6999-4553;
e-mail: lena.platova2015@yandex.ru

Olga I. Kauseva, Ultrasound Diagnostics Doctor;
ORCID: 0000-0002-7117-7642;
eLibrary SPIN: 5387-8115;
e-mail: olga.kauseva@gmail.com

ОБ АВТОРАХ

***Нариманова Метанат Рафиговна,** канд. мед. наук, доцент;
адрес: Россия, 117513, Москва, ул. Островитянова, д. 1/6;
ORCID: 0000-0003-0677-2952;
eLibrary SPIN: 2723-5711;
e-mail: safarovametanat@yandex.ru

Доброхотова Юлия Эдуардовна, д-р мед. наук, профессор;
ORCID: 0000-0002-7830-2290;
eLibrary SPIN: 2925-9948;
e-mail: pr.dobrohotova@mail.ru

Хачатрян Азнар Сааковна, канд. мед. наук, доцент;
ORCID: 0009-0000-2767-8995;
eLibrary SPIN: 7707-5981;
e-mail: aznardoc@yahoo.com

Ильина Ирина Юрьевна, д-р мед. наук, профессор кафедры;
ORCID: 0000-0001-8155-8775;
eLibrary SPIN: 5753-4380;
e-mail: iliyina@mail.ru

Ибрагимова Джамиля Магомедовна, канд. мед. наук, доцент;
ORCID: 0000-0002-8738-868X;
eLibrary SPIN: 7962-4941;
e-mail: dgam81@mail.ru

Платова Елена Сергеевна, канд. мед. наук, доцент;
ORCID: 0009-0009-6999-4553;
e-mail: lena.platova2015@yandex.ru

Каусева Ольга Игоревна, врач ультразвуковой диагностики;
ORCID: 0000-0002-7117-7642;
eLibrary SPIN: 5387-8115;
e-mail: olga.kauseva@gmail.com

*Corresponding author / Автор, ответственный за переписку