Revista de Ciencias Médicas de Pinar del Río

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S2): e7088

REVIEW ARTICLE

Red degeneration of uterine leiomyomas during pregnancy: literature review

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Received: December 30, 2025
Accepted: December 31, 2025
Published: December 31, 2025

Citar como: Núñez-Arroba S del P, Burgasi-Quimbita AE, Castañeda-Menta JT, Andrade-Chisag HV. Degeneración roja de leiomiomas uterinos durante el embarazo: análisis bibliográfico. Rev Ciencias Médicas [Internet]. 2025 [citado: fecha de acceso]; 29(S2): e7088. Disponible en: http://revcmpinar.sld.cu/index.php/publicaciones/article/view/7088

ABSTRACT

Introduction: uterine leiomyomas are among the most frequent benign neoplasms in women of reproductive age. During pregnancy, they may undergo degenerative changes, with red degeneration being an uncommon variant that generates relevant obstetric complications.
Objective: to analyze the available evidence on red degeneration of uterine leiomyomas in pregnant women, describing their clinical, diagnostic, and therapeutic management characteristics.
Methods: a systematic review of the scientific literature was conducted across several databases. The search was performed using an algorithm with keywords and Boolean operators, allowing the identification of relevant sources. Selected studies, after applying inclusion and exclusion criteria, were critically analyzed considering timeliness, methodological quality, and thematic relevance.
Development: the reviewed studies show that red degeneration occurs in a small percentage of fibroids during pregnancy, mainly presenting with acute abdominal pain and characteristic findings on ultrasound and magnetic resonance imaging. Conservative management, focused on pain control and prenatal monitoring, is usually sufficient in most cases. However, complications such as preterm birth, fetal growth restriction, and higher cesarean rates are reported. Surgery is reserved for emergency situations due to maternal-fetal risk. A multidisciplinary approach and close follow-up are essential to optimize clinical outcomes.
Conclusions: red degeneration of uterine leiomyomas during pregnancy, although infrequent, represents a significant clinical challenge. Timely diagnosis through imaging and conservative management help reduce risks, although an increase in obstetric complications persists.

Keywords: Pregnancy Complications, Neoplastic; Pregnancy; Leiomyoma; Uterine Neoplasms.

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S2): e7088

INTRODUCTION

Uterine fibroids are one of the most common benign neoplasms in women of reproductive age, with a prevalence reaching up to 70 % in women aged 45. They originate from smooth muscle cells of the myometrium and are classified according to their location as subserosal, intramural, transmural, and submucosal, with subserosal fibroids being the most common. They can also be located in adjacent structures such as the broad ligament, fallopian tubes, or cervix. Their growth is influenced by estrogen, which explains their tendency to increase in size during the reproductive years and decrease after menopause.(1)

Regarding their morphological characteristics, leiomyomas exhibit variations related to cell arrangement, mitotic rate, and their relationship to blood vessels. These alterations are observed in approximately 30 % of cases, most frequently after age 40. Furthermore, myomas can undergo various degenerative changes, including apoplexy, atrophy, and hyalinization, the latter being the most common. A particular variant is red degeneration, which occurs primarily during pregnancy and manifests clinically as acute abdominal pain.(2)

In the long term, fibroids undergoing red degeneration can progress to peripheral calcification, especially in elderly women. Another less frequent form of degeneration is necrosis, present in approximately 10 % of cases, which may be associated with pregnancy and childbirth. These morphological and degenerative variations not only enrich the understanding of the pathophysiology of leiomyomas, but also have relevant clinical implications, particularly in the obstetric and gynecological context, where they can generate complications requiring a multidisciplinary approach.(3)

In relation to the above, the present review is carried out, which aimed toTo analyze the available evidence on red degeneration of uterine leiomyomas in pregnant women, describing their clinical and diagnostic characteristics and therapeutic management options.

METHODS

This study was designed as a systematic literature review, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure transparency and methodological rigor. The search period was limited to the years 2010 to 2024, thus encompassing the most recent and relevant scientific literature on red degeneration of uterine leiomyomas during pregnancy.

The information search was conducted in various internationally recognized and widely used electronic databases, including PubMed, SciELO, ScienceDirect, Google Scholar, LILACS, and BVSALUD. Secondary references from relevant articles were also reviewed, and grey literature (theses, technical reports, and institutional documents) was considered when it provided pertinent clinical or epidemiological data. This strategy broadened the range of sources and reduced publication bias.

The search strategy was constructed by combining keywords and MeSH/DeCS descriptors related to "uterine leiomyoma," "red degeneration," and "pregnancy," using Boolean operators (AND, OR, NOT) to optimize record retrieval. Articles in Spanish, English, and Portuguese were included to encompass the scientific output of Latin America and the international community. Inclusion criteria included studies published within the defined time frame, peer-reviewed articles, and

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S2): e7088

works that directly addressed the topic of uterine leiomyomas with red degeneration in pregnant women. Duplicates, articles without full-text access, irrelevant studies, studies outside the search period, and publications in languages other than those considered were excluded.

The selection process was carried out in several stages: first, titles and abstracts were read to discard irrelevant records; subsequently, the full texts of potentially eligible articles were reviewed. Initially, approximately 350 records were identified, of which, after cleaning and removing duplicates, 37 articles remained. Finally, 13 studies that met all the inclusion criteria were included.

For data extraction and analysis, a matrix was designed to collect key variables from each study: author, year of publication, methodological design, sample characteristics, and main clinical outcomes. The information was synthesized qualitatively, as the heterogeneity of the studies precluded a quantitative meta-analysis. Nevertheless, a comparative analysis of the findings was performed, highlighting common patterns and differences among the reviewed studies. This methodology allowed for the integration of the available evidence and provided a critical and up-to-date perspective on red degeneration of uterine leiomyomas during pregnancy.

DEVELOPMENT

Uterine leiomyomas are benign tumors that originate in the smooth muscle cells of the uterus, also known as the myometrium. Their location can vary, occurring within the myometrium, on the endometrial surface (submucosal), in the outer layer of the uterus (subserosal), or embedded in the uterine wall (intramural). The size of these lesions is heterogeneous, ranging from small nodules with no clinical impact to large masses capable of distorting the uterine anatomy and compromising adjacent pelvic organs. Clinically, although they remain asymptomatic in many cases, they can manifest with significant symptoms such as menorrhagia, pelvic pain, a feeling of pressure on neighboring structures (bladder or rectum), and even infertility, which underscores their importance in gynecological practice.[4,5]

Uterine leiomyomas can undergo different types of degeneration, with red degeneration being one of the most common. Degeneration refers to morphological and structural changes within the tumor that can alter its appearance and behavior; these can be:[6,7]

- Red degeneration, also known as hyaline degeneration, is a process in which necrosis of the smooth muscle cells of the leiomyoma occurs, followed by hemorrhage within the tumor. This can lead to a change in the tumor's appearance, which takes on a reddish color due to the presence of clotted blood.
- Hyaline Degeneration: In this type of degeneration, the smooth muscle cells of the leiomyoma undergo hyaline transformation, in which homogeneous, hyaline substances accumulate in the cell cytoplasm. This may be due to a decrease in blood supply to the tumor.
- Cystic Degeneration: In some cases, leiomyomas can develop fluid-filled cystic areas within the tumor tissue. These areas may result from the degeneration of muscle cells or from the accumulation of fluid in intercellular spaces.
- Fatty Degeneration: This is less common and occurs when the smooth muscle cells of the leiomyoma transform into fat cells, leading to the formation of adipose tissue within the tumor.

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S2): e7088

These degeneration mechanisms can occur simultaneously or sequentially in a uterine leiomyoma and can influence the clinical presentation and management of the condition. Red degeneration, in particular, can be relevant during pregnancy, as it can be associated with complications such as acute uterine hemorrhage.[6]

Risk factors for developing uterine leiomyomas during pregnancy include various biological conditions and personal histories. Age is a determining factor, as women of reproductive age, particularly between 30 and 50, are more likely to develop these tumors. There is also a clear genetic predisposition, with those having a family history of uterine fibroids showing an increased risk. Ethnic origin also plays a significant role, with a higher prevalence observed in women of African descent compared to other groups. Obesity has been linked to an increased risk, probably due to elevated levels of circulating estrogen in overweight or obese women, which promote tumor growth. Regarding parity, some studies suggest that nulliparous women or those with fewer children may have a slightly higher risk of developing leiomyomas, while multiparity is associated with a protective effect. Finally, hormonal changes, both those inherent to pregnancy and those resulting from hormone replacement therapy, directly influence the appearance and growth of these tumors, with estrogens being recognized as a stimulating factor in the development of fibroids.[1,3]

During pregnancy, uterine leiomyomas can undergo significant changes due to the hormonal and hemodynamic changes associated with gestation. Some women experience an increase in the size of their leiomyomas during the first trimester due to increased levels of estrogen and progesterone, hormones involved in uterine tissue growth. However, in many cases, leiomyomas remain stable in size or may even decrease in size during pregnancy due to the redistribution of uterine blood flow and the influence of placental hormones, such as placental lactogen and progesterone.[6]

Despite these changes, in some cases, leiomyomas can experience significant growth during pregnancy, which can increase the risk of obstetric and gynecological complications, such as miscarriage, preterm birth, abnormal fetal presentation, placenta previa or accreta, and complications during labor and delivery. Careful obstetric monitoring and multidisciplinary management are essential to ensure a favorable outcome for both mother and fetus in pregnant women with uterine leiomyomas.
Red degeneration of uterine leiomyoma can have a significant impact on pregnancy, as it can be associated with several complications for both the mother and the fetus.[8] Among the main complications are:[7]

- Acute uterine bleeding: Red degeneration involves necrosis and hemorrhage within the tumor, which can result in acute uterine bleeding. This bleeding can be severe and require urgent medical intervention to control it and prevent complications such as acute maternal anemia.
- Acute abdominal pain: This can be accompanied by acute and severe abdominal pain. This pain can interfere with maternal well-being and affect the quality of life of the pregnant woman.
- Miscarriage: In severe cases, especially if massive bleeding occurs, there is an increased risk of miscarriage or pregnancy loss. The bleeding and associated physiological stress can trigger uterine contractions and cervical dilation, which can lead to pregnancy loss.
- Obstetric complications: This pregnancy may increase the risk of obstetric complications, such as premature birth, abnormal fetal presentation, placenta previa or accreta, and complications during labor and delivery. These complications can endanger the health of both the mother and the fetus and may require specialized obstetric care.
- Need for medical or surgical intervention: In some severe cases of red degeneration, medical or surgical interventions may be necessary to control bleeding, relieve pain, or preserve

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S2): e7088

maternal and fetal health. These interventions may include administering medications to stop the bleeding, uterine artery embolization to reduce blood flow to the leiomyoma, or even surgical removal of the tumor.

The diagnosis and management of uterine leiomyomas with red degeneration during pregnancy are essential to ensure maternal and fetal health. Some diagnostic strategies and management options that may be considered are described here:[4,9]

- Clinical examination: The diagnosis of uterine leiomyomas during pregnancy usually begins with a clinical examination performed by an obstetrician-gynecologist. During this examination, palpable uterine masses may be detected, which may suggest the presence of leiomyomas.
- Imaging: Imaging techniques such as ultrasound and magnetic resonance imaging (MRI) are useful for confirming the diagnosis of uterine leiomyomas and evaluating their size, location, and characteristics. Red degeneration may appear as hyperechoic or heterogeneous areas on ultrasound and as areas of high signal intensity on T1- and T2-weighted MRI.

Its clinical management includes:[1,2]

- Prenatal monitoring: Pregnant women with uterine leiomyomas and red degeneration should undergo careful prenatal monitoring to track tumor progression and detect any potential complications. This may include regular ultrasound examinations to assess leiomyoma growth and fetal health.
- Pain management: Management of pain associated with red degeneration may include the use of pain relievers that are safe during pregnancy and non-pharmacological measures such as applying localized heat or a comfortable position to relieve discomfort.
- Hemorrhage control: In cases of acute uterine bleeding due to red degeneration, medical treatment may be necessary to control the bleeding and stabilize the patient. This may include the administration of hemostatic agents, blood transfusions, or uterine arterial embolization in severe cases.
- Surgical considerations: In severe or complicated cases of uterine leiomyomas with red degeneration during pregnancy, surgical intervention may be necessary. However, surgery during pregnancy is generally reserved for emergency situations due to the potential risk to the fetus. The decision to perform surgery during pregnancy should be carefully evaluated by a multidisciplinary team including obstetricians, surgeons, and anesthesiologists.
- Management of childbirth: The delivery plan for women with uterine leiomyomas and red degeneration should be individualized based on the location, size, and characteristics of the tumor, as well as maternal and fetal health. In some cases, a cesarean section may be necessary instead of vaginal delivery to avoid obstetric complications related to the leiomyomas.

In general, the management of uterine leiomyomas with red degeneration during pregnancy requires a comprehensive assessment of the risks and benefits of different management options, with the goal of optimizing maternal and fetal outcomes. A multidisciplinary approach and open communication between healthcare providers and the patient are essential for making informed decisions and providing safe and effective care. Considerations for obstetric management and delivery planning in women with uterine leiomyomas during pregnancy should be carefully considered and tailored to each individual case.[4]

Knowing the location and size of uterine leiomyomas is essential to determining the most appropriate delivery plan. Submucosal leiomyomas can increase the risk of complications during vaginal delivery, such as obstruction of the birth canal or retained placenta, while intramural or subserosal leiomyomas may not have a significant impact on the delivery process.[4]

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The risk of obstetric complications associated with uterine leiomyomas, such as miscarriage, preterm birth, abnormal fetal presentation, placenta previa or accreta, and complications during labor and delivery, should be assessed. This risk may vary depending on factors such as the location and size of the leiomyoma, as well as maternal and fetal health.[1,2]

Birth planning should be individualized and discussed in detail with the patient and her healthcare team. In some cases, a cesarean section may need to be considered instead of a vaginal delivery to minimize the risk of obstetric complications related to leiomyomas. However, in many cases, a safe and successful vaginal delivery is possible with careful assessment and management of risk factors.[1,2,5]

During labor and delivery, fetal monitoring is essential to identify signs of distress and allow for timely obstetric decisions, including continuous monitoring of fetal heart rate and assessment of labor progress. Simultaneously, the risk of uterine hemorrhage must be considered, especially in cases of leiomyomas with red degeneration or significant growth during pregnancy, adopting preventive measures such as the use of hemostatic agents and preparation for blood transfusions. Finally, clear and transparent communication with the patient and her family is indispensable to ensure informed consent, after a detailed discussion of the risks, benefits, and alternative obstetric management options. [5,10]

The findings of this review confirm that uterine leiomyomas are a common entity in women of reproductive age, but red degeneration in the context of pregnancy is relatively rare. This underscores the importance of accurate and timely diagnosis.[11] Ultrasound remains the first-line diagnostic tool, although magnetic resonance imaging can provide additional information and is particularly useful in complex cases. Conservative management is generally successful in most cases, with pain relief as the primary therapeutic goal. The findings reinforce the idea that surgery during pregnancy should be avoided whenever possible due to the risks to both the mother and the fetus. The association of red degeneration with obstetric complications highlights the need for rigorous prenatal monitoring.[12,13]

CONCLUSIONS

Uterine leiomyoma with red degeneration is a rare but clinically relevant condition during pregnancy. Diagnosis is primarily based on imaging studies such as ultrasound and magnetic resonance imaging (MRI), and it is characterized by specific symptoms such as acute abdominal pain and uterine tenderness. Management is usually conservative, focusing on pain control and maternal-fetal monitoring, although in severe cases surgical intervention may be required, with the associated risks for both mother and fetus. Most women with this complication can carry their pregnancy to term with appropriate management, although there is an increased risk of obstetric complications such as preterm birth and the need for cesarean section. However, despite advances in diagnosis and treatment, further research is still needed to fully understand the pathophysiological mechanisms of red degeneration and its long-term impact on maternal and fetal health.

ISSN: 1561-3194 **RNPS:** 1877
Rev Ciencias Médicas. 2025; 29(S2): e7088

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