Review Article

The meaning and management of uterine fibroids in pregnancy: a narrative review of the literature

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Background and Objective: To evaluate and write a narrative review of the literature about the meaning of uterine leiomyomas and their fate during pregnancy, on the other, to which extent these tumors are capable of affecting pregnancy outcomes. Nowadays, it is commonly accepted that fibroids can cause slight or no increased risk fo bad obstetric outcome. Although decreased uterine distensibility or mechanical obstruction may explain some adverse outcomes, the precise mechanism by which uterine fibroids induce obstetric complications is not clear.

Methods: A narrative review of the literature to gather the researches about the fibroid and pregnancy coexistence with the pregnancy outcomes by searching computerized databases, hand searches, and authoritative texts.

Key Content and Findings: An overview of the fibroids and pregnancy coexistence were systematically examined. The behavior of the fibroids during the early and late pregnancy periods was discussed. Studies that advocate the fibroid presence has a negative effect on the early and late pregnancy processes, and studies that against to these outcomes were mentioned. The reported complications and the management options of these complications were discussed. At last, besides the delivery timing and options, the fibroid treatment options during the pregnancy period were also discussed.

Conclusions: Due to the different scenarios on the pregnancy outcomes with the coexistence of fibroids and pregnancy. This narrative review provides a vision for the clinicians in both having information about the meaning of the fibroids during the pregnancy period and having information for providing counseling to couples who wish to have a pregnancy or who are waiting a baby at any gestational weeks.

Keywords: Fibroids; pregnancy; pain during pregnancy

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Introduction

Uterine fibroids are the clonal formation of the mesenchimal cell line that turns into tumor formation in either location (submucous, intramural, subserous and serous) at the uterus. Due to their asymptomatic nature and commonness; it is reported to be detected in about 3–12% of pregnancy cases (1,2). The fibroid volume changes were reported to be differed according to the fibroid size at the early antenatal period. The fibroids that are small in size (diameter ≤1 cm) have a tendency to increase in volume;

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Table 1 Sources used for this overview

MEDLINE search between 1950 and January 2023. Keywords: fibroid in pregnancy, pregnancy follow-up with fibroids, pregnancy outcomes with fibroids, fibroid treatment during the pregnancy
PubMed search between 1950 and January 2023. Keywords: fibroid in pregnancy, pregnancy follow-up with fibroids, pregnancy outcomes with fibroids, fibroid treatment during the pregnancy. Hand searches of the references of retrieved literature
Personal and college libraries searching for texts on research methods and literature reviews
Discussions with experts in the field of reviews of the literature

stay at the same size in volume measured to be 1 to <3 cm; tendency to decrease in volume measured to be ≥3 cm, during the pregnancy (3). The fibroids that did increase in size mostly grew at the first trimester and remain stable during the other trimesters, interestingly nearly 10–12% of the fibroids regress (4-8). Regardless of their growth pattern, the relationship between uterine fibroids and adverse pregnancy outcome is not clearly understood. In a very early report, it was mentioned that nearly 10% to 30% of women with uterine fibroids had faced with obstetric complications (5). In the current literature, there is a need for a review that provides information about the effects of fibroids on pregnancy from many different perspectives.

This narrative review is aimed to provide information about the meaning of uterine leiomyomas, their fate during pregnancy, and on the other, the prognostic factors of these tumors for affecting the pregnancy outcomes. We present this article in accordance with the Narrative Review reporting checklist (available at https://gpm.amegroups.com/article/view/10.21037/gpm-22-4/rc).

Methods

Information used to write this narrative review was collected by using the keywords: fibroid in pregnancy, pregnancy follow-up with fibroids, pregnancy outcomes with fibroids, fibroid treatment during the pregnancy, via the medical digital data-base systems (*Table 1*). The synonym word myoma is also used for the search instead of fibroid. We searched PubMed and MEDLINE for researches from 1950 through January 2023. The researches that were obtained after the search steps that were written in *Table 1* were included in this narrative review. The researches that were written in languages other than English and missing data about the pregnancy outcomes were excluded from the study.

Discussion

Pregnancy with accompanying fibroids may behave differently in different periods of pregnancy. At this point, we structured the discussion to include the changes that occur during early pregnancy and late pregnancy period. We mentioned the possible effects on the mode of delivery. The management alternatives regarding the management of the problems that fibroids may cause were also discussed. The associations between fibroids and frequently seen pregnancy outcomes are summarized in *Table 2*.

Early pregnancy

Miscarriage

In the current literature, the spontaneous miscarriage rates were detected to be increased in pregnant women with fibroids, other than the fibroid size the number and the location of the fibroids were stated to have a link with the rate of the miscarriages (6,7). The location of the fibroid may also be important. Early miscarriage is more common in women with fibroids located in the uterine corpus (body) than in the lower uterine segment. Similarly, the miscarriage risk is increased with the submucosal fibroids [odds ratio (OR): 3.85, 95% confidence interval (CI): 1.12–13.27] (8). The mechanism by which fibroids cause spontaneous abortion is unclear. Increased uterine irritability and contractility with the compressive effect of fibroids can compromise the blood supply of the decidua and the developing placenta. This situation is presented with subchorionic hematoma, bleeding or miscarriage during the early pregnancy (6-8).

Genetic screening tests and diagnostic testing

There is no data about the linkage between maternal fibroids with the fetal chromosomal abnormalities but the placental function could be affected due to location or size

Table 2 Frequently seen obstetric outcomes of the fibroids with the pregnancy period

Complication/symptom	Incidence with fibroid	Incidence without fibroid	Study
Miscarriage	14–23.6%; submucosal fibroids (OR: 3.85, 95% CI: 1.12–13.27) for miscarriage	12–18%	Benson *et al.* [2001], Shavell *et al.* [2012] (6,7)
Bleeding early pregnancy	4–5%	2–3%	Benson *et al.* [2001], Shavell *et al.* [2012] (6,7)
PPROM	6.2%	12.2%	Stout *et al.* [2010], Klatsky *et al.* [2008], Ezzedine *et al.* [2016] (1,9,10)
Preterm labor	16.1%	8.7%	Stout *et al.* [2010], Shavell *et al.* [2012], Klatsky *et al.* [2008], Ezzedine *et al.* [2016] (1,7,9,10)
Placental detachment	2–2.5%	0.9%	Ezzedine *et al.* [2016] (10)
Placenta previa	1.4–1.8%	0.6%	Ezzedine *et al.* [2016] (10)
IUGR	11–13%	8.6–9%	Klatsky *et al.* [2008], Coronado *et al.* [2000], Ezzedine *et al.* [2016] (9-11)
Malpresentation	8–10.5%	4.5%	Stout *et al.* [2010], Klatsky *et al.* [2008] (1,9)
Breech	5–6%	1–2%	
Dysfunctional labor	7–8%	3.1%	Klatsky *et al.* [2008], Coronado *et al.* [2000] (9,11)
Cesarean delivery	23–73%	13–30%	Qidwai *et al.* [2006], Donnez *et al.* [2002] (12,13)
Post-partum bleeding	2.5–4%	1.4%	Klatsky *et al.* [2008], Coronado *et al.* [2000], Chuang *et al.* [2001], Chen *et al.* [2021], Qidwai *et al.* [2006], Donnez *et al.* [2002], Burton *et al.* [1989], Ezzedine *et al.* [2016] (9-16)
Uterine rupture after myomectomy	NA	0.5–1%	Levine *et al.* [1997], Dubuisso *et al.* [2000] (17,18)
Pain	23–30%	10%	Klatsky *et al.* [2008] (9)

OR, odds ratio; CI, confidence interval; PPROM, preterm premature rupture of membranes; IUGR, intra-uterine growth restriction; NA, not available.

of the fibroids. Fibroids may interfere with normal placental implantation and may have an effect on the possible cell turnover for the fibroids itself may have an effect on the genetic screening tests that are arranging during the pregnancy period.

The effect on the either biochemical genetic screening mom values or fetal cell-free DNA testing on the fetal fraction is not well known (19-21). There are researches needed to be organized for searching the effect of fibroids on the genetic screening tests.

Also, the size or location of the fibroid may cause difficulty for the genetic diagnostic testing. Especially for the chorionic villus sampling, in cases where fibroids located close to the placenta even causing the test not to be performed (22).

Bleeding in early pregnancy

The location and the number of the fibroids had an effect on early pregnancy bleeding. If the placenta implants close to the fibroid compared with pregnancies in which there is no contact between the placenta and fibroid, the reported bleeding incidence was increased by two times (14% *vs.* 7.6%), with multiple fibroids the risk was increased nearly by three times (23.6% *vs.* 8%) (5-8). In some cases, these heavy bleedings may have a linkage with adverse pregnancy outcomes during the late pregnancy period (5,9).

Late pregnancy

Preterm labor and preterm premature rupture of membranes (PPROM)

Pregnant women with fibroids are significantly more likely to develop preterm labor and to deliver preterm than women without fibroids (1,9). Multiple fibroids and fibroids that have a close relation to the placenta appear to

be an independent risk factor for preterm labor; additively, fibroids that are more than 5 cm in size are having increased risk of preterm delivery (7,9). It should be kept in mind that iatrogenic attitude for excising fibroids with cesarean section could be one of these differences. In contrast, fibroids do not appear to be a risk factor for PPROM. Interestingly, it was reported that fibroids are associated with a decreased risk of PPROM (9). Although there are publications on the fact that fibroids reduce the risk of PPROM, more data are needed to prove this association.

Placental detachment

Contrary to the debatable data, current literature suggests that the risk of placental detachment is increased 3–4 times in women with fibroids (9). The locations of the fibroids such as submucosal, retroplacental and intramural close to the endometrial cavity (with proximity up to 2 mm) were reported to have independent risk for placental detachment (8).

Red degeneration

Unspecified intense abdominal pain during late pregnancy, especially with uterine fibroid, is a difficult condition in both defining and treating the origin of the pain. Red degeneration is one of the less common causes of the intense abdominal pain by comparing to appendicitis, renal stones and ovarian torsion during late pregnancy. The incidence of the red degeneration is not well known. The data about red degeneration is gathered from the case reports. Red degeneration is commonly detected in women having fibroids larger than 5 cm and the propose mechanism is prostaglandin discharge secondary to hypoxia and necrosis of the fibroid. The diagnosis could be done by magnetic resonance imaging (MRI) scan with specific changes, a peripheral high-intensity on T1-weighted images confined to the thrombosed numerous dilated vessels surrounding the fibroid (23). The released substances are thought to cause excessive pain with uterine contractions that may result with placental detachment. Symptomatic treatment painkillers with fluid replacement is a good choice before deciding on surgery (11).

Placenta previa and placental insertion pathologies

There are few studies observing the association between fibroids and placental insertion and adhesion pathologies. It was suggested that the presence of fibroids is resulted in a 2–3 times increased risk of placental pathologies (5,11). Fibroids located in the lower uterine segment bare increased risk for placenta previa (1).

Intra-uterine growth restriction

It is commonly thought that uterine fibroids have a linkage with diminished fetal growth. However, the evidence-based data suggests that fetal growth does not appear to be affected by the presence of uterine fibroids (9,11,13,14) Besides to the cumulative data and a population-based study suggested that women with fibroids are at slightly increased risk of delivering a growth-restricted infant, these results were not adjusted for maternal age or gestational age (9,24). The mechanic problems that may cause compression to the endometrial cavity has an impact on the fetal skeletal development; including, dolichocephaly (lateral compression of the fetal skull), torticollis (abnormal twisting of the neck), and limb reduction defects (15,25).

Preeclampsia

It can be thought that fibroids during the early pregnancy periods may adversely affect the trophoblast invasion and may cause preeclampsia, the disease characterized by abnormal trophoblast invasion, at the later weeks of pregnancy. However, studies reported so far claim that there is no association of uterine fibroids and preeclampsia (1-9,14,22,24-26). However, a newly reported prospective study claims that the presence of fibroids increases the risk of high blood pressure in pregnancy (adjusted hazard radio: 2.95, 95% CI: 1.35–6.44). However, the size, number, and location of fibroids were not addressed in this study design (26). Therefore, it is not clear whether the presence of fibroids increases the risk of preeclampsia.

Labor and delivery

Malpresentation, labor dystocia, and cesarean delivery

The location, amount, and size of the fibroids may have a link with increased risk of fetal malpresentation (1,9,24). Large fibroids, multiple fibroids, and fibroids in the lower uterine segment have all been reported as independent risk factors for malpresentation (8,9,11,12,14,15,23-26). The incidence of breech presentation was reported to be nearly 5–6% in cases with uterine fibroids, without fibroids the incidence is nearly 2–3% (1,5,9,23). There is no enough data about the other malpresentation incidence with the uterine fibroids.

The number of deliveries via cesarean section was reported to be increased with uterine fibroids. One of the components is fetal malpresentation, large fibroids, multiple fibroids, submucosal fibroids and fibroids in the lower uterine segment are considered predisposing

factors for cesarean delivery (8,11,13,16). Despite the increased risk of cesarean deliveries, the presence of uterine fibroids-even large fibroids (>5 cm)-should not be regarded as a contraindication to a trial of labor (11,24). Even after excluding pregnancies with breech presentation and placenta previa, which would by routine standard of care require a cesarean delivery, the pregnancies with uterine fibroids were reported to be high (1,8,9,11-16,23-26). In the current literature, the location (especially low segment) and the number of fibroids may interfere with effective labor contractions. In a population-based study reported risk for the dysfunctional labor with uterine fibroids was (OR 1.85, 95% CI: 1.26–2.72) (24). In addition, decreased oxytocinase activity due to the fibroids at the uterus, leads a contractile uterus and inability to relax. It is thought that higher uterine tonus may interfere fetus to reach the ideal labor position; resulting not only increase frequency of the breech presentation but also increase the frequency of cephalopelvic disproportion (9,11,12,24,26). Also, the attitude of the surgeons towards doing myomectomy simultaneous with the cesarean section may also be a factor for the increased cesarean section rates.

Postpartum hemorrhage

During the involution phase after delivery, fibroids may distort the uterine architecture and interfere with myometrial contractions, which can result in uterine atony and postpartum hemorrhage. The data about this association are not clear (8,9,11,12,14,15,23-27). Observational studies reported a substantial number of postpartum hysterectomy cases in women who have uterine fibroids after delivery (8-10,27). Pooled cumulative data suggest that postpartum hemorrhage is significantly more likely in women with fibroids compared to control subjects (2.5% *vs.* 1.4%, respectively (9). Due to the same mechanisms, rest placenta was also reported to be high in cases having uterine fibroids in either location (8-16,23-27).

Uterine rupture after myomectomy

Uterine rupture after abdominal myomectomy is extremely rare (27-29). The focus of discussions on this subject based primary on the uterine repair method after the fibroid excision. The risk of uterine rupture increases with the use of excessive energy, single layer myometrial closure, leaving a dead space after the closure and the hematoma formation secondary to an inadequate hemostasis (17). In a retrospective study of 120 women delivering at term following abdominal myomectomy in which the uterine cavity was not entered, there were no cases of uterine rupture reported (30). Whether the same is true also of laparoscopic myomectomy; the absolute risk of uterine rupture following laparoscopic myomectomy remains low at 0.5% to 1% (18,31). Recent data suggest that such uterine ruptures occur prior to the onset of labor or during the third trimester at the site of the prior myomectomy (17,18,27-31). To estimate the possible risk of uterine rupture, the repaired myometrial part should be learned and examined with the transvaginal ultrasound during the early pregnancy period. In case of suspicion of loose healing repeated transvaginal ultrasound examination at all trimesters can be preferred. As the uterine rupture risk increases at the third trimester, careful myometrial assessment with the transvaginal sonogram should be preferred for detecting an early uterine rupture or determining the delivery time.

Management of fibroids

Pre-pregnancy period

In cases, where the presence of fibroids is thought to be an obstacle to a pregnancy, a surgical approach can be recommended for couples who want to conceive. Mostly submucous, intramural fibroids that make compression to the endometrial cavity can adversely affect the fertility conditions. For the other fibroids; such as subserous, intramural without doing any compression to the endometrial cavity, surgical removal is not generally recommended (32). Secondly, for the fibroids causing excessive bleeding, pain and adverse effect on the quality of life, surgical treatment options come into forefront for the treatment.

The need of myomectomy for protecting adverse pregnancy outcomes before pregnancy is debatable (33,34). Unfortunately, there are not enough data favoring doing or not doing myomectomy for this issue. Case by case interpretation based with patient previous pregnancy history, size, number and the location of the fibroids and besides sonohysterogram or hysterosalpingopraphy may provide information for deciding the management options.

Pain management

Due to the enlargement of both uterus and fibroids, the blood perfusion to the fibroid could be diminished resulting with red degeneration or torsion of the fibroid (3-6). This can happen mostly at late first trimester or early second trimester and more commonly seen in cases having fibroid length more than 5 cm (7-9). Mild leukocyte elevation

with nausea or vomiting may accompany the pain. The prostaglandin secretion secondary to the degeneration is the pathophysiology. For the management supportive care with resting and oral hydration is the first step (8,12). Acetaminophen is the first line drug option if necessary opioids can be added to the treatment. Nonsteroid anti-inflammatory drugs (NSAIDs) can be considered before 32 weeks of gestation but the premature closure of the ductus arteriosus, oligohydramniosis or fetal/neonatal platelet dysfunction can be seen (5). In case of prolong usage (more than 2 days) of the NSAIDs close ultrasound follow-up (weekly) can be performed for assessing these side effects (3,5,12). Interval treatment can be considered in cases of unwanted effects of the treatment. Alternatively, surgery can be considered in cases with emergent conditions such as, fibroid torsion, mechanical compression causing obstruction to the adjacent structures or desperate medical treatment taking very long period of time (35-37). Excising the fibroids during pregnancy is not a common intervention because of possible complications; namely, excessive bleeding, early delivery, abortus, and uterine rupture. In the current literature, there are limited data about fibroid excision during pregnancy. At the reported data miscarriage rate is nearly 5%, the median gestational age at delivery was 38 weeks mostly with cesarean section (37) with acceptable pregnancy outcomes. However, retrospective study design and limited patient numbers are making a need of prospective studies that can give idea about the effectiveness and safety of the procedure. Transvaginal excision of the fibroids that arises from the uterine cervix is another procedure. It is recommended not to excise asymptomatic fibroids. In case of hemorrhage, urinary tract obstruction, infection and intense pain, excision can be considered with taking the risks of hemorrhage, rupture of membranes, and/or pregnancy loss (38).

Although there are reviews written so far about the coexistence of uterine fibroids and pregnancy; major strength of our narrative review is that there are not many articles that comprehensively examine the coexistence of uterine fibroids and pregnancy. However, the majority of the articles that we used while creating this narrative review, were at a retrospective design. Unfortunately, there are not enough randomized controlled studies on this subject. Considering the problems caused by the archiving and recording system, this situation constitutes the most important limitation of our review. However, when both situations are considered together, this review is valuable as it gives insight into the meaning of uterine leiomyomas, their fate during pregnancy and, on the other, to which extent these tumors are capable of affecting pregnancy outcomes. The future researches needed to be done at a prospective randomized and controlled design.

Conclusions

Unfortunately, we still do not have clear information about the course of each fibroid and effects on the pregnancy outcome. Because a certain part of the fibroids that exist at the antenatal course are not noticed or incidentally detected at some time during the process or firstly seen at the cesarean section. Fibroids that were detected before pregnancy or at the beginning of the follow-up period are the cases providing information about the effect of fibroids on the pregnancy outcome. In the light of this data, the complications caused by fibroids during pregnancy are not only related to the size and location of the fibroids, but also related to the molecular and enzymatic reactions. With this combined effect, single and large fibroids (>3 cm in diameter), as well as multiple and lower uterine segment fibroids, are causing increased risk of early pregnancy loss, preterm labor and birth, placental detachment, fetal presentation anomalies, placental insertion problems, labor complications (dysfunctional contractions, postpartum bleeding). On the other hand, the risk of pre-eclampsia and intrauterine growth retardation were not detected to be increased with the fibroids.

Although fibroids cause fear during the pregnancy follow-up period, the majority of the fibroids stay without causing any adverse pregnancy outcomes. Because of this, the pregnancy follow-up planning can be considered within the general obstetrics principles and the delivery choice firstly considered via vaginal birth. Couples with a known uterine fibroid should be informed about the meaning and management of uterine fibroids in pregnancy; besides, counseling about the pain resulting from the fibroids should also be given during the early pregnancy period.

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Footnote

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