UTERINE MYOMAS AND PREGNANCY: EFFECTS AND COMPLICATIONS: REVIEW ARTICLE

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Abstract:
Fibroid in pregnancy is common in clinical obstetric practice. The topic is becoming more relevant in contemporary obstetrics due to the demographic shift towards delayed childbearing, the rising rate of obesity, and many pregnancies occurring after the treatment of fibroids. However, there are conflicting reports in the literature on many so-called fibroid complications in pregnancy, and there are inadequate data on the optimum management strategy. An evidence base is lacking on the pregnancy outcome of many conventional and newer treatment modalities of fibroids. This review addresses the characteristics and behaviour of fibroids during pregnancy, their incidence and demography, diagnosis, the complications that can arise during pregnancy and their antenatal management, the labour pattern, mode of delivery and the postpartum course, with critical appraisal of the literature together with certain special situations such as pregnancy after various types of myomectomy and uterine arterial embolisation.

Keywords: Fibroid and pregnancy, leiomyoma.

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Introduction:

The origin of leiomyomas is not totally understood, and their pathophysiology is probably multifactorial. A genetic incident triggers the onset of the disease and different types of myomas may develop by diverse molecular pathways. Additionally, a hormonal influence is also present; estrogens and progesterone have a key role in the growth and maintenance of lesions ***(1).***

Because of the hormonal status and vascular changes typical of gestation, practitioners and patients are often afraid of the accelerated growth of fibroids during pregnancy, and of its consequences. Moreover, it is a common belief that uterine leiomyomas, mainly those which distort the endometrial cavity, may impair fertility, and cause adverse reproductive outcomes such as miscarriage, preterm labor, and placental abruption (***2).***

Effect of pregnancy on fibroid:

Effect on size:

Given the hormonal dependence of fibroids, it is expected that pregnancy would promote their growth. However, ultrasound studies have shown that most fibroids do not actually increase in size. Many authors have shown a trimester dependent fibroid growth in pregnancy: during the first trimester fibroids of all sizes either remained unchanged or increased in size, a possible early response to increased oestrogen ***(3).***

During the second trimester, smaller fibroids (2–6 cm) usually remain unchanged or increased in size, but those larger than 6 cm became smaller, probably resulting from the initiation of oestrogen receptor downregulation. Regardless of initial size, during the third trimester, fibroids usually remained unchanged or decreased in size, reflecting again oestrogen receptor downregulation ***(4).***

A reduction of the fibroids to their pre-pregnancy size usually occurs weeks after delivery. No relationship has been found between the initial fibroid volume and fibroid growth during gestational weeks. Recent studies even showed a pregnancy related reduction in women with ultrasonically diagnosed fibroid during pregnancy ***(5).***

Effect on shape:

Because they tend to become soft in pregnancy as a result of interstitial oedema, fibroids may flatten out and become indistinct. Subserous fibroids may be easily palpated as the uterus enlarges and may on occasion be mistaken for fetal parts ***(6).***

Effect of parity on fibroid:

In most epidemiological as well as cohort studies, parity has been shown to be associated with reduced fibroid risk (adjusted for age, body mass index, smoking, alcohol, and other reproductive co-variables such as infertility) ***(7).***

Fibroid risk is lower among women who have undergone more recent pregnancies than with remote pregnancies. Studies reporting data on miscarriage or induced abortion show little or no evidence of the protective effect of early pregnancy on fibroids. The protective effect is therefore likely to be linked in some way to events that occur in late pregnancy, at delivery or during the postpartum period, although the precise mechanism is unknown ***(8).***

Pregnancy before 25 years may occur before the development of the fibroids, and conception after 30–35 years may be associated with already grown fibroids which may be too large to regress by the remodelling process. The expected greatest protective effect of parity would be for pregnancies during the mid reproductive years (between 25–29 years of age) ***(9).***

Effect of inter-pregnancy interval on fibroid:

The protective effect of second and subsequent pregnancies depends on the intervals between the previous pregnancies. Short intervals provide little additional protection (***10).***

Likewise, intervals that are too long may also have little effect, because the fibroids that develop after a previous pregnancy over a long period of time may grow beyond the critical size that may not be susceptible to remodelling. However, the specific inter-pregnancy interval for this effect, or lack of, on fibroid size regression has not been defined ***(11).***

Effect of fibroid on pregnancy:

Fibroids are usually asymptomatic during pregnancy. The most important factors in determining morbidities in pregnancy include fibroid number, size, location, and relation to placental implantation (retroplacental). Submucous fibroids have the strongest association with lower ongoing pregnancy rate, mainly due to defective implantation. However, there is no evidence that subserous or intramural fibroids adversely affect pregnancy outcome ***(1).***

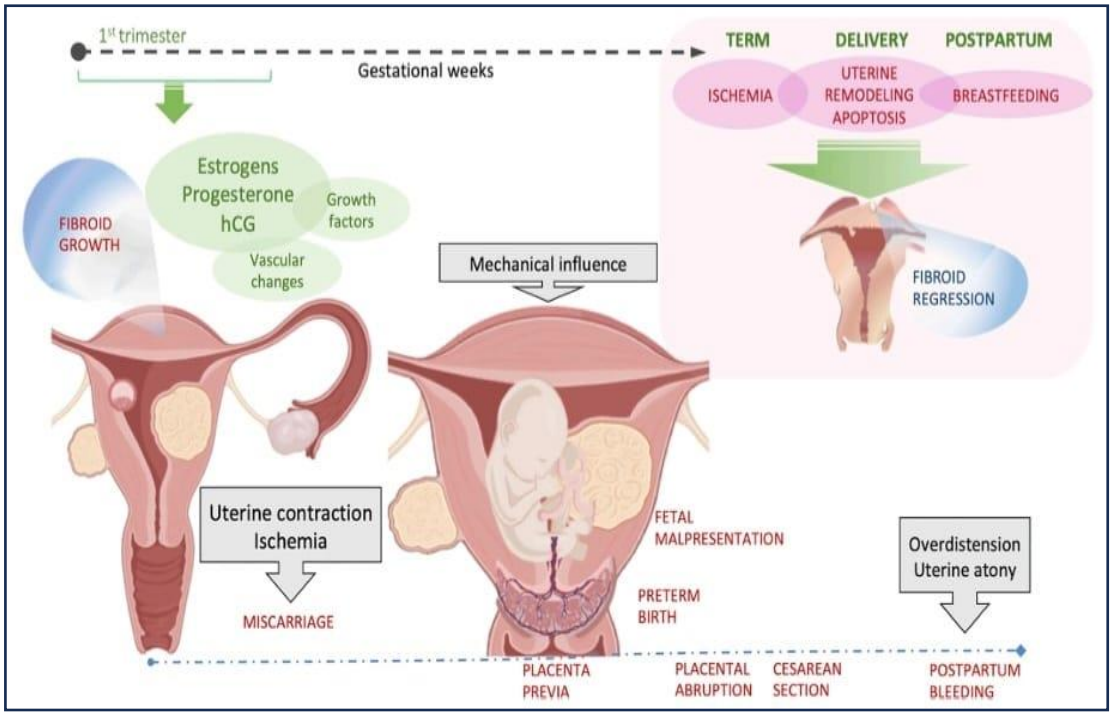

Figure (1): Putative mechanisms of fibroid growth during gestation and the effects of uterine fibroids on obstetric outcomes by interfering in placentation, fetal position, uterine distension, myometrial contractility, and postpartum hemostasis ***(12).***

Large submucous or multiple fibroids may distort the uterine cavity leading to abnormal lie and presentation, pre-labour premature rupture of the membranes (pPROM), pre-term labour (PTL) and risk of CS. Cervical or low anterior fibroids may obstruct labour and render CS technically difficult. Retroplacental fibroids have been shown to be associated with a higher incidence of miscarriage, PTL, placental abruption, and postpartum haemorrhage (PPH) ***(10).***

Pressure symptoms:

There may be increased frequency of micturition due to bladder irritation by an anterior cervical fibroid, aided by increased vascularity in the early weeks of pregnancy. Occasionally, pressure on the bladder neck can cause urinary retention; if untreated, this can progress to overflow incontinence ***(2).***

Pain is the most common complication of fibroid in pregnancy, with 5–15% of women with fibroids requiring hospitalization at some point ***(3).***

The risk of pain increases with size and is high with fibroids >5 cm in diameter. It is interesting that, in the same woman, fibroids can cause severe pain in one pregnancy yet no pain in the next. Pressure on the fibroid itself can cause a dull ache. Torsion of a pedunculated fibroid is more likely to occur in the first trimester and after delivery, when there is enough space in the abdomino-pelvic cavity to permit a high risk of twist of the free and mobile fibroid on its pedicle ***(13).***

Fibroid may undergo various types of degenerations such as hyaline, calcareous, fatty, myxomatous, and red degenerations. Red degeneration of fibroid (carneous degeneration) is rare to occur and it has been mentioned that it occurs during pregnancy but rare in non pregnant women, Three main theories have been proposed to explain the severe pain associated with red degeneration. First, that rapid fibroid growth results in the tissue outgrowing its blood supply leading to tissue anoxia, necrosis, and infarction***. (14).***

Second, that the growing uterus result in a change in the architecture (kinking) of the blood supply to the fibroid leading to ischemia and necrosis even in the absence of fibroid growth. ***(15).***

Third, that the pain results from the release of prostaglandins from cellular damage within the fibroid. This is supported by the observation that ibuprofen and other prostaglandin synthetase inhibitors effectively and rapidly control fibroid pain ***(16).***

Red degeneration, also known as carneous degeneration, is one of four main types of degeneration that can involve a uterine leiomyoma. While it is an uncommon type of degeneration, it is thought to be the most common form of degeneration of a leiomyoma during pregnancy ***(17).***

Carneous degeneration is a subtype of hemorrhagic infarction of leiomyomas that often occurs during pregnancy. On gross pathology, it is characterized

by a red (hemorrhagic) appearance of the leiomyoma. Red degeneration primarily occurs secondary to venous thrombosis within the periphery of the tumor or rupture of intra tumoral arteries ***(18).***

Red or carneous degeneration is the most specific complication of fibroid in pregnancy, occurring in about 5% of cases, most commonly in the first and early second trimester which corresponds with the greatest fibroid growth ***(5).***

Red degeneration due to its red color appearance on examination—makes up only 3% of all uterine fibroids, but it accounts for 8% of tumors in pregnancy. It may be a troublesome cause of pregnancy complications, such as severe pain, in many women ***(19).***

Clinically, the condition is characterized by focal abdominal pain of acute onset, mild fever, nausea and vomiting, localized tenderness over the fibroid, rebound tenderness, and leucocytosis. However, a white cell count <10×106/l is not uncommon and rebound tenderness can be frequently absent. Therefore, a diagnosis other than red degeneration must be considered. Differential diagnoses include appendicitis, PTL, placental abruption, ureteric stone, or pyelonephritis ***(20).***

Fibroids, labour, and delivery:

In non-pregnant women, clinical experimental studies using an intrauterine micro-transducer catheter before and after myomectomy have shown that fibroids may disturb spontaneous uterine contractions as well as its responsiveness to oxytocin and vasopressin, which may be regulated up to 70% by myomectomy ***(21).***

Kinematic evaluation of uterine contractions by cine MR imaging in non-pregnant women has demonstrated partial interruption of uterine peristalsis by submucous fibroids, but not by intramural or subserous fibroids, suggesting dysfunctional uterine contractility which may be related to pregnancy loss in patients with submucous fibroids ***(6).***

It is postulated that a similar decrease in the force of uterine contractions or disruption of the coordinated spread of contractile waves may occur during labour, and lead to dysfunctional labour. However, published reports in the literature are rather conflicting. The increased prevalence of dysfunctional and prolonged labour found by some authors has not been confirmed by others ***(11).***

Most importantly, it is not known what effect, if any, the uterine contractions caused by fibroid(s) would have on the fetal heart rate pattern in labour. It is the general clinical experience that the uterus with fibroid(s) is no less responsive to the use of oxytocics (e.g., prostaglandins for induction of labour, oxytocin for stimulation of labour, carboprost or misoprostol for the treatment of PPH) than its non-fibroid counterpart ***(8).***

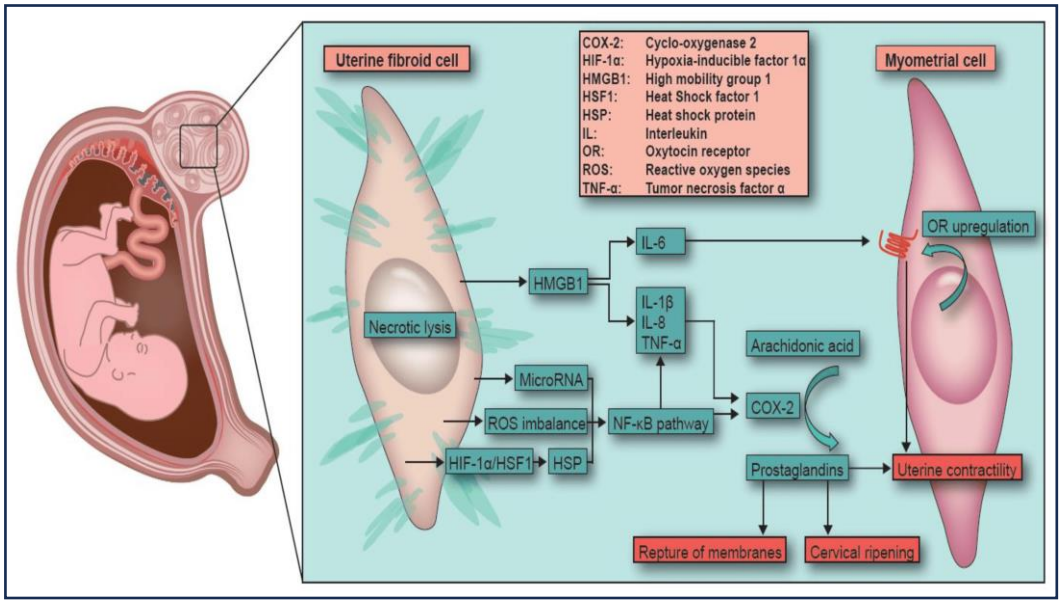

Figure (2): Fibroid necrosis during pregnancy. Schematic representation of the hypothesized inflammatory pathway of necrosis and induction of pre-term labor in women with fibroid necrosis during pregnancy ***(22).***

Risk and incidence of caesarean delivery in fibroid pregnancy:

Although many women with fibroids achieve normal vaginal deliveries, several recent studies have shown a higher rate of CS in women with fibroids than in those with normal uteruses. The fibroid size, but not the number, has been shown to be associated with the higher CS rate, although the

critical offending size differed between studies, from 5 cm diameter57 to 10 cm ***(1).***

Fibroids and postpartum haemorrhage:

Several studies have reported an increased risk of atonic PPH following vaginal delivery, especially if the fibroids are >3 cm and retroplacental. Others, however, have not reported any PPH. Pooled cumulative data
suggest that PPH is significantly more likely in women with fibroids compared with controls ***(10).*** The risk is higher in caesarean delivery. Decreased force and an uncoordinated pattern of uterine contractions are thought to be the pathophysiological mechanisms behind PPH ***(23).*** However, it is difficult to explain how effective and coordinated uterine contractions during labour that achieve a normal delivery would revert to an uncoordinated pattern to cause PPH just because of fibroids, unless there are other contributing factors such as prolonged labour, intrapartum oxytocin stimulation, increased maternal age, uterine distension, etc. Retained placenta is more common in all women with fibroids regardless of the location of the fibroid ***(20).***

Fate of fibroids after delivery:

As discussed earlier, fibroids may regress after delivery. However, torsion may complicate a pedunculated fibroid. Ischaemic degeneration of a submucous fibroid due to reduced blood supply during puerperium may provide an ideal culture medium for anaerobic organisms ***(2).***

Rarely, sloughing and necrosis of a puerperal submucous fibroid can occur with fever and tachycardia. This should be differentiated from retained products of conception by thorough clinical examination and use of appropriate diagnostic imaging***(13).***

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