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Review Article

Safety of pregnancy in uterine fibroids

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ABSTRACT

Uterine fibroid is one of the most common intrauterine masses among females at the reproductive age. Pregnancy and uterine fibroids are highly correlated. Pregnancy-related hormones influence the size of uterine fibroids, and fibroids have many impacts on pregnancy. Although most if the uterine fibroids are asymptomatic during pregnancy, serious complications may occur. The main complications include abortion, premature rupture of membranes, premature labor, abruptio placentae, peripartum hemorrhage, fetal malpresentation, fetal intrauterine growth retardation, small for gestational age infants, and fetal anomalies. The main risk factors for complications are related to the fibroid number, size, volume, location, and type. Large, multiple, retroplacental, submucosal, subserosal, pedunculated, or low-lying fibroids carries the highest risk for complications during pregnancy. This review will address the prevalence of uterine fibroids during pregnancy, its effects, and complications.

Keywords: Complications, Effect, Fibroid, Pregnancy, Safety, Uterine fibroid

INTRODUCTION

Uterine fibroid (also known as leiomyomas) is one of the most common intrauterine masses prevalent among women in reproductive age. It is estimated that it affects 40-60% of women at the age of 35 years and up to 80% of women at the age of 50.¹

Uterine fibroids are benign tumors arising from the smooth muscles of the uterus. Although most of the uterine fibroids are asymptomatic, women begin to complain of the them when they increase in size or develop any complications, and the hormonal changes during pregnancy are one of the main conditions that lead increase the fibroid size.² During pregnancy, the

diagnosis of fibroids remains challenging. Less than one half of the large fibroids (42%), and less than one eighth of the small fibroids (12.5%) can be palpated by physical examination.³ Furthermore, ultrasound examination only reveals 1.4-2.7% of uterine fibroids.⁴

The effect and safety of uterine fibroids on pregnancy has been a topic of concern for decades. Researchers report conflicting opinions about this issue.

Some studies indicate that most of the fibroids are asymptomatic during pregnancy and are associated to safe uneventful pregnancy and labor, whilst others argue that uterine fibroids are sometimes associated with deleterious complications during pregnancy and/or labor

and, therefore, should be managed preconceptionally. This article will review the prevalence, effects and complications, and safety of uterine fibroids on pregnancy.

Prevalence of uterine fibroids among pregnant women

The exact prevalence of uterine fibroids is not accurately determined. This is partly due to the asymptomatic nature of the vast majority of the fibroids, and partly due to the difficult diagnosis as previously mentioned. However, the prevalence of uterine fibroids during pregnancy reported in some studies ranges from 1.6 to 10.7%, and the prevalence varies from one semester to another.^{1,5} The first trimester of pregnancy has the highest prevalence rate because some fibroids increase in size during this semester.⁶

On the other hand, in an attempt to explore the effect of uterine fibroids on infertility rates, the incidence of fibroids was found to range from 12 to 25% among women with infertility. However, a direct causal-effect relationship between fibroids and infertility could not be established.^{7,8}

Diagnosis of uterine fibroids among pregnancy

During pregnancy, the vast majority of fibroids remain asymptomatic. Symptoms occur when the fibroid increases in size or develop complications. When uterine fibroids expand in size, they exert a mass effect on their blood vessels supply leading to ischemia, anoxia, and necrosis. Cell necrosis and damage are associated with increased prostaglandin release and subsequently localized pain. Another cause of necrosis is the large expansion of fibroid in size without a similar increase in blood flow, leading to a mismatch between the vascular demand of the tissue and the available blood supply.⁹ Furthermore, severe localized pain also arises from torsion of pedunculated sub-serosal uterine fibroids or from impaction of uterine fibroids compromising adjacent blood vessels.³ Therefore, pain is the most common presentation of large (>5 cm) or complicated uterine fibroids during pregnancy.^{7,9} Other less common symptoms include pelvic pressure, vaginal bleeding, urinary frequency, and constipation.^{7,10} The large-sized fibroids exert pressure effects on nearby organs as well. Anterior cervical fibroids compress the urinary bladder leading to frequent micturition. Sometimes, partial obstruction may result if compression occurred on bladder neck leading to urine retention.

Physical examination of uterine fibroids has a limited value. Only less than half of the large fibroids (>5 cm) can be revealed on physical examination.⁴ Smaller fibroids (3-5 cm) have only a 12.5% chance to be detected by physical examination.³ Ultrasonography can diagnose only 1.4-2.7% of uterine fibroids during pregnancy. Fibroids appear on ultrasonography as spherical mass lesions that are echogenically-

distinguishable from surrounding uterine myometrium.¹¹ The size, site, number, and some complications are assessed by ultrasound examination. Some ultrasonographic features of the tumor were reported to be associated with the clinical presentation. For instance, Leav-Toaf et al, in their ultrasonographic study on 113 pregnant women, found that among the 10 women who had cystic changes or heterogenous echogenic pattern of their fibroid, 7 (70%) had severe localized abdominal pain.¹² And in comparison, with the 11.7% (12 out of 103) who had abdominal pain without cystic changes or heterogenous echogenic patterns, the differences were statistically significant ($p < 0.05$).¹²

Effect of pregnancy on uterine fibroids

The main effect of pregnancy on fibroid is related to the size of the uterine fibroids. It has been argued for many decades whether the hormonal changes occurring during pregnancy can influence the size of uterine fibroids or not. For a couple of decades, uterine fibroids were thought to enlarge during pregnancy, particularly during the first trimester of pregnancy. Many studies and review articles agreed with this theory. Benaglia et al, in their prospective cohort study on 25 women with fibroids and 25 controls, reported that the size of the fibroids increased dramatically (more than double the original size) during the first 7 weeks of gestations.¹³ Similarly, Rosati et al. reported a significant increase in size of uterine fibroids (of more than 8%) during early pregnancy ($p < 0.001$).¹⁴ Similarly, Neiger et al. indicated that the pre-pregnant size of uterine fibroid was about 88% of the pregnant size among the studied women.¹⁵

The pregnancy-related size growth of uterine fibroids is largely attribute to the hormonal changes occurring during pregnancy. Estrogen is claimed to be the principle hormone promoting uterine growth.¹⁶ Progesterone is thought to be responsible for maintain the size of these tumors.¹⁷ However, sex hormone did not seem to be the only hormones involved. This is because the growth of uterine fibroid does not follow the same pattern of progressively increasing secretion of estrogen and progesterone i.e. a linear relationship between fibroid growth rate and sex hormone secretion had never been established.^{14,16} Although estrogen and progesterone increase steadily during pregnancy, fibroids shrink in size during second and third trimesters.^{12,14,16,18}

Therefore, authors argue a role of other hormones in fibroid growth during pregnancy particularly human chorionic gonadotropin (hCG).¹⁹ The rapid increase in serum hCG occurring during the initial pregnancy may be responsible for the initial increase in size of the uterine fibroid noted during early pregnancy.

On the other hand, some studied reported that up to 78% of uterine fibroids do not show significant growth during pregnancy.^{14,20} The remaining ~22% increased 12.5-25% of their initial size during the first 10 weeks of gestation.

Effects of uterine fibroids on pregnancy

The impact of uterine fibroids on pregnancy has been a matter of concern for years. Although most of the uterine fibroids are asymptomatic and result in uneventful pregnancy and labor, complications are not uncommon. Pain is often the presenting symptom that warrants searching for uterine fibroids complications. This section will review the mechanism of effects, the complications, and safety of uterine fibroids on pregnancy

Mechanism of uterine fibroid effects on pregnancy

The mechanisms whereby uterine fibroids may lead to complications are not fully established. It is argued that the dramatic increase in size lead to compromising the blood supply and subsequent ischemic necrosis of the tumor. This results in pain, vaginal bleeding, and pelvic heaviness. The prostaglandin release resulting from tissue damage results in further increase in pain and uterine contractions.^{7,9}

Other mechanisms involved include mechanical effects of uterine fibroids on fetal sac. The size, site, number, type (subserosal, intramural, or submucosal), and shape (sessile or pedunculated) are responsible for various mechanisms of adverse effects.⁴ For instance, subserosal fibroids are at risk for torsion and red degeneration, lower-located fibroids (i.e. near cervix) might result in obstructed labor, submucosal fibroids are associated with higher miscarriage rates, and large-sized fibroids (>5 cm) are associated with uterine cavity distortion, abnormal fetal position, and presentation.²¹⁻²³

Complications

Though rare, uterine fibroids are associated with significantly higher risk of complications during pregnancy and labor when compared to healthy women. Uterine fibroids, particularly those of submucosal origin, are associated with high risk of abnormal fetal position and presentation. It is estimated that uterine fibroids are associated with 13% risk for breech presentation, 19% risk for pre-term labor and premature rupture of membranes, 49% risk for cesarean delivery, and 8% risk for abortion, antenatal hemorrhage, postpartum hemorrhage, abruptio placentae, and labor dystocia.²³

Abortion is often associated with submucosal fibroids. It is estimated to occur in 14% of pregnant females with fibroids in comparison to 7.6% in healthy pregnant women. The main determinant for abortion is the location of the fibroid. Abortion was reported to be 8 times more common among pregnant ladies with retroplacental fibroids than those with non-retroplacental fibroids.²⁴ Abruptio placentae occurs due to impaired blood flow to the placenta and adjacent uterine myometrium. Therefore, it often with submucous, large (>7.8 cm or >200 ml volume), or retroplacental fibroids.²⁵ Preterm labor and premature rupture of membranes (PROM) are other

significant complications of uterine fibroid. They are associated with retroplacental large fibroids (3.6 cm).^{12,14,24} Although significant, preterm labor was estimated to be only 2 or 3 weeks prior to the expected date of delivery which does not have a significant impact on the fetus.²⁶

Other complications include fibroid torsion and red degeneration, fetal anomalies, fetal growth restriction, fetal demise, and preeclampsia. Fibroid torsion often occurs during the first trimester when there is an adequate intrauterine space for peduncular twist. It results from pedunculated subserosal types of uterine fibroid. The main risk factor for uterine fibroid torsion is rapid body movements. Red degeneration results from this torsion and is estimated to have a prevalence of 5% during pregnancy.²⁷ It presents clinically with severe abdominal pain, nausea, vomiting, fever, local tenderness and rebound tenderness.⁸

Fetal lie and malpresentation are common consequences of uterine distortion. Breech presentation and oblique lie are the most common abnormalities encountered; and they are associated with large (>5cm), multiple, and lower-lying fibroids.²⁸ Other reported fetal complications reported are small for gestational age infants, intrauterine growth retardation, and rarely fetal anomalies. The fetal anomalies noted with uterine fibroids were congenital torticollis, head deformities, and limb reduction defects.^{26,27}

CONCLUSION

Pregnancy and uterine fibroids are highly correlated. Pregnancy-related hormones influence the size of uterine fibroids, and fibroids have many impacts on pregnancy. Although most if the uterine fibroids are asymptomatic during pregnancy, serious complications may occur. The main complications include abortion, premature rupture of membranes, premature labor, abruptio placentae, peripartum hemorrhage, fetal malpresentation, fetal intrauterine growth retardation, small for gestational age infants, and fetal anomalies. The main risk factors for complications are related to the fibroid number, size, volume, location, and type. Large, multiple, retroplacental, submucosal, subserosal, pedunculated, or low-lying fibroids carries the highest risk for complications during pregnancy.

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