Peer Review File

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Reviewer Comments

Comment 1: Line 25-26: you can't say that, not enough study.

Reply 1: Dear Reviewer, Line 25-26 is changed and written as "The fate of the pregnancy with uterine fibroids is debatable. Although decreased uterine distensibility or mechanical obstruction may be thought to cause some adverse problems, the mechanisms that can affect the pregnancy outcome is still mystery."

Comment 2: Line 51: it is not true, your ref (1988!)

see: Comparison of uterine fibroid' growth pattern during pregnancy according to fetal sex, Delli CarpiniG et all. Bio sex Differ. 2019. Use FIGO (>2011) as you can.

Reply 2: Dear Reviewer, Line 51 is opted with a different and updated reference: Mitro SD, Peddada S, Chen Z, Buck Louis GM, Gleason JL, Zhang C, Grantz KL. Natural history of fibroids in pregnancy: National Institute of Child Health and Human Development Fetal Growth Studies - Singletons cohort. Fertil Steril. 2022; 118(4):656-65.

It is written that "The fibroid volume changes reported to be differed according to the fibroid size at the early antenatal period. The fibroids that are small in size (diameter ≤ 1cm) have a tendency to increase in volume; stay at the same size in volumes measured to be 1 to <3 cm; tendency to decrease in volumes measured to be ≥3 cm, during the pregnancy"

Comment 3: Line 128-129: Red degeneration is not well known and requires a separate chapter. Please read the case report: seeing red degeneration in uterine fibroids in pregnancy: proceed with caution. Cerdeira AS et al. Lancet. 2019.

Reply 3: Dear Reviewer. Separate chapter for the red degeneration is added the main document labeled with 2.3

"**2.3 Red Degeneration.** Unspecified intense abdominal pain at the 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 at the 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 5cm 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 (15). The released substances are thought to cause excessive pain with uterine contractions that may result with placental detachment. Symptomatic treatment pain killers with fluid replacement are a good choices before deciding surgery (16).

Comment 4: Line 140-141: no true, old bibliography. MRI is useful in case of problems and complications.

Reply 4: Dear Reviewer. The line 140-141 is stating that It is commonly thought that uterine fibroids have a linkage between diminished fetal growth. However, the evidence-based data suggests that fetal growth does not appear to be affected by the presence of uterine fibroids. MRI may not be used for defining the growth pattern of the baby. Bibliography about the fibroids with fetal growth retardation is updated according to your recommendations.

Comment 5: Table 2 is very good but you have to be more specific about miscarriages, because the differences are significant.

Reply 5: Dear Reviewer. For the miscarriages the information about the miscarriage risk with submucosal fibroids is added to the table 2 as “the miscarriage risk is increased with the submucosal fibroids (OR:3.85 CI(1.12-13.27))”

Comment 6: The conclusion section should be re-written and revised to give the last and updated knowledge about the issue.

Reply 6: Dear Reviewer. The conclusion is re-written and revised according to the last and updated knowledge about this issue. As “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 exists 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 (> 3cm 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 on the pregnancy follow-up period, majority of the fibroids are 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 at the early pregnancy period."

Comment 7: The references later than 2000's should be opted.

Reply 7: Dear reviewer references later than 2000's are opted