Reviewer A

This retrospective study including patients with adenomyosis has to many variables to allow a scientific conclusion. A much more detailled description should be given of the adenomyotic lesions: an enlarged uterus can be due to the presence of diffuse adenomyosis or focal adenomyosis; each of them can have a different impact.

Secondly the selection of patient to be pre treated or not is not clear and when not randomised there will be a bias in the selection of patients to be treated or not. Furthermore transfers probably are performed on with embryo's i a different stage of development (day 3><day 5).

There is also a difference in the time of suppression with the GnRha before ET.

More details how the uterus is measured should be given.

also a comparison with a control group could be included stratified for age, treatment....

More data should be given on the patients'characteristics in both groups

check paper by native English speaking person

Comment 1: A much more detailled description should be given of the adenomyotic lesions: an enlarged uterus can be due to the presence of diffuse adenomyosis or focal adenomyosis; each of them can have a different impact.

Reply 1: We have added ultrasound descriptions about adenomyosis lesions (focal/diffuse), and compared the distribution of different types of adenomyosis (focal/diffuse) between GnRH-a treatment group and GnRH-a-free group, which found no differences between two groups.

Changes in the text: we added some data in the method (see Page 6-7, line 116-121) and table1.

Comment 2: Secondly the selection of patient to be pre treated or not is not clear and when not randomised there will be a bias in the selection of patients to be treated or not.

Reply 2: Firstly, for infertile patients with adenomyosis with small uterine volume, the decision to pretreat with or without GnRH-a is a combination of different clinicians' experience as well as the patient's wishes and the patient's schedule. Some patients required direct embryo transplantation and refused GnRH-a pretreatment, while others required GnRH-a pretreatment followed by transplantation. According to whether patients had GnRH-a pretreatment before the FET cycle, this study divided the FET cycles into two groups: (i) GnRH-a treatment group and (ii) GnRH-a-free treatment group. **Secondly,** this study was a retrospective cohort study. There was indeed a bias caused by the inability to randomize patients. On the basis of our this retrospective cohort study, we can design a follow-up randomized controlled study to further verify this conclusion.

Changes in the text: we have modified our text as advised (see Page 7, line 122-132).

Comment 3: Furthermore transfers probably are performed on with embryo's i a different stage of development (day 3><day 5).

Reply 3: No statistic difference was observed in transferred embryo (Cleavage embryo/ Blastocyst) between two groups (see Table 1).

Changes in the text: we have modified our text as advised (see Page 9, line 179-184 in Results part, and table 1).

Comment 4: There is also a difference in the time of suppression with the GnRha before ET.

Reply 4: Firstly, in the GnRH-a treatment group, patients with adenomyosis were pretreated with 1-3 GnRH-a injections before FET (every 28 days): the percentage of cycles with one, two and three GnRH-a injections before FET was 4/45 (8.9%), 15/45 (33.3%) and 26 /45 (57.8%), respectively. **Secondly,** the total number of cycles of GnRH-a pretreatment was 45 cycles, so due to the limited sample size we did not analyze the effects of the time of suppression with the GnRH-a before FET on pregnancy outcomes. However, according to our study, although the pretreatment time of GnRH-a was different, the reproductive outcome of the GnRH-a treatment group was superior to that of the GnRH-a-free treatment group.

Changes in the text: we have modified our text as advised (see Page 9, line 172-176 in Results part).

Comment 5: More details how the uterus is measured should be given.

Reply 5: All TVS were performed by two highly skilled radiologists. The main criteria for sonographic diagnosis of adenomyosis included a globular uterus or asymmetric myometrial thickening; heterogeneous myometrium, with thin "venetian blind" shadows between areas of increased echogenicity; myometrial cysts; indistinctness of the margins of the endometrium and echogenic linear striations; and nodules extending from the endometrium into the myometrium. TVS was conducted before GnRH-a pretreatment and 28 days after the last GnRH-a injection (before commencing FET cycle) for patients with GnRH-a pretreatment. For patients without GnRH-a pretreatment, TVS was conducted before commencing FET cycle. The volume of uterus was calculated by using a geometric formula for prolate ellipsoid volume: long diameter × width diameter × anteroposterior diameter × π/6. Furthermore, type of adenomyosis was divided into focal, diffuse according to the adenomyotic lesions. Focal adenomyosis (including adenomyoma) is classified when typical ultrasonographic adenomyotic signs are circumscribed in aggregates and surrounded by normal myometrium, while diffuse adenomyosis when typical alterations at TVS spread throughout the myometrium.

Changes in the text: we added a paragraph to describe ultrasound measurement in method part (see Page 6-7, line 105-121).

Comment 6: Also, a comparison with a control group could be included stratified for age, treatment….

Reply 6: Thank you very much for the advice. **Firstly,** the total number of FET cycles pretreated with GnRH-a in our study was 45 cycles, and the sample size of GnRH-a treatment group after stratification would have been smaller, which would not be suitable for subgroup analysis after stratification due to the limited sample size and low power. **Secondly,** from our present study, the reproductive outcome of the GnRH-a treatment group was still significantly better than that of GnRH-a-free treatment group after correction for confounding factors **by using logistic regression**, and the difference was statistically significant. Both univariate analysis and multivariate analysis confirmed the effect of GnRH-a pretreatment on improving pregnancy outcomes in patients with adenomyosis infertility.

Changes in the text: results of multivariate analysis are shown in results part (see Page 9-10, line 185-198) and table 2.

Comment 7: More data should be given on the patients'characteristics in both groups

Reply 7: We have also added the following patients' characteristics in both groups: duration of infertility, gravidity times, parity times, adenomyotic lesions (diffuse/ focal). And No statistic difference was observed in those characteristics between two groups.

Changes in the text: we added some data in the results (see Page 9, line 179-184) and table1.

Comment 8: check paper by native English speaking person

Reply 8: This paper was edited by one or more of the highly qualified native English speaking editors at AJE (see editing certificate).

Changes in the text: we have modified our text as advised (see editing certificate).

Reviewer B

It is a clinically interesting paper that GnRHa administration before ET to the uterus suffering from adenomyosis increases pregnancy rate and live birth rate, and even though there is no significant change in uterine volume. These facts are limited to cases of a particular uterine volume, but both are new discoveries. However, there are some problems with the description of research results. First, the definitions of the GnRHa-treated group and the control group are not described in methods of the main chapter (eg, whether it is the number of cycles or the actual number of people). In addition, although the characteristics of both groups are shown in Table 1, there are many results in which the% calculation method is incorrect. Furthermore, the items that should be described in "Results" are not described, while the results of the items that are not described in "Methods" are described in "Results". There are some other amendments, and if all of them are amended, this paper will be worth publishing.

Below is a list of points to consider.

Comment 1: The criteria for selecting cases with and without GnRHa are unclear. Should be clarified.

Reply 1: For infertile patients with adenomyosis with small uterine volume, the decision to pretreat with or without GnRH-a is a combination of different clinicians' experience as well as the patient's wishes and the patient's schedule. Some patients required direct embryo transplantation and refused GnRH-a pretreatment, while others required GnRH-a pretreatment followed by transplantation. According to whether patients had GnRH-a pretreatment before the FET cycle, this study divided the FET cycles into two groups: (i) GnRH-a treatment group and (ii) GnRH-a-free treatment group.

Changes in the text: we have modified our text as advised (see Page 7, line 122-132).

Comment 2: Patients in the GnRHa-administered group are receiving long-acting GnRHa, but the drug name, dosage, and administration method should be stated.

Reply 2: Patients in GnRH-a treatment group were injected subcutaneously with long-acting GnRH-a (Triptorelin Acetate for Injection, Ipsen, French, 3.75mg) for three months, starting from the 1st day to the 5th day of menstruation, once per 28 days.

Changes in the text: we have modified our text as advised (see Page 7, line 132-135).

Comment 3: "The inclusion criteria", "Exclusion criteria" and "The pregnancy outcome" are

listed with (number) in the head, but they are confused because they are the same as the notation in the cited references. A different notation should be used.

Reply 3: We have modified our text as advised.

Changes in the text: we have modified our text as advised (see Page 5-6, line 97-104, and Page 8, line 145-146).

Comment 4: Continuous variables are stated to have been analyzed by t-test or nonparametric test, but nonparametric tested items should be listed as "median (range)" rather than "mean ± standard deviation".

Reply 4: We have modified our text as advised.

Changes in the text: we have modified our text as advised (see table 1).

Comment 5: [Result] The description method is unclear. First, the number of people in both groups (number of cycles?) should be listed, and then the outcomes of each group: number of pregnancies (pregnancy rate), number of miscarriages (miscarriage rate) and number of births (birth rate). After that, each result should be compared and the presence or absence of a significant difference should be stated.

Reply 5: We have modified our text as advised.

Changes in the text: we have modified our text as advised (see Page 9-10, line 167-202).

Comment 6: [Result] shows the results of comparing the uterine volume before and after GnRHa administration in the GnRHa-administered group, so the comparison method should be described in [Method]. The timing should be stated when the ultrasonography was performed. Was GnRHa given immediately after the end, when the endometrium was 8 mm, or at the time of transplantation? It should be clarified whether it was done immediately after the last GnRHa administration, when the endometrium was 8 mm, or at the time of transplantation. What is the test method used for the comparison?

Reply 6: We have modified our text as advised. **Firstly**, In GnRH-a treatment group, uterine volume before and after GnRH-a pretreatment were also compared by t-test. **Secondly**, TVS was conducted before GnRH-a pretreatment and 28 days after the last GnRH-a injection (before commencing FET cycle) for patients with GnRH-a pretreatment. For patients without GnRH-a pretreatment, TVS was conducted before commencing FET cycle. **Thirdly**, patients in GnRH-a treatment group were injected subcutaneously with long-acting GnRH-a for three months, starting from the 1st day to the 5th day of menstruation, once per 28 days. Endometrial preparation was started 28 days later after the last GnRH-a injection with daily estradiol 4-6mg, and progesterone was added when the thickness of endometrial reached 8mm. After 5-7 days of progesterone treatment, one or two embryos were transferred into the uterine.

Changes in the text: Firstly, as for " 【Result】 shows the results of comparing the uterine volume before and after GnRHa administration in the GnRHa-administered group, so the comparison method should be described in [Method]" and "What is the test method used for the comparison?", we have modified our text (see Page 8, line 162-163). **Secondly**, as for "The timing should be stated when the ultrasonography was performed", we have modified our text (see Page 6, line 111-114). **Thirdly**, as for "Was GnRHa given immediately after the end…. or at the time of transplantation", we have modified our text (see Page 7, line 132-140).

Comment 7: [Table 1] Why are Maternal age and Paternal age not shown as mean (or median)? On the other hand, the method of calculating% of each item (< 35 and ≥35) is incorrect. "Primary infertility", "Secondary infertility", "Cleavage embryo" and "Blastocyst" have made same mistakes. Please refer to the table below.

Reply 7: Thank you so much for your detailed and patient guidance. We have modified our text as advised. Maternal age and Paternal age have been shown as mean ± standard deviation.

Changes in the text: we have modified our text as advised (see table 1).

Comment 8: [Table 1] BMI, AMH, and FSH should have their official names listed in the bottom column of the table. Please refer to the table below.

Reply 8: Thank you so much for your detailed and patient guidance. We have modified our text as advised.

Changes in the text: we have modified our text as advised (see table 1).

Table 1

Characteristics	GnRH-a treatment (n= a)	GnRH-a-free treatment (n= A)	P value
Maternal age (years)			0.149
< 35	b (b/a %)	B (B/A %)	
≥35	a-b (a-b/a %)	B (A-B/A %)	
Paternal age (years)			0.191
< 35	c (c/a %)	C (C/A %)	
≥35	a-c (a-c/a %)	A-C (A-C/A %)	
Infertility type （%）			0.097
Primary infertility	d (d/a %)	D (D/A %)	
Secondary infertility	a-d (a-d/a %)	A-D (A-D/A %)	
Uterine volume	81.3±13.1	78.9±11.7	0.220
BMI （kg/m2）	23.9±3.9	23.0±4.1	0.184
AMH	3.36±2.6	3.50±2.9	0.873
FSH	6.52±1.5	6.53±2.2	0.985
Endometrial thickness (mm)	10.0±2.2	10.0±1.7	0.964
No. of embryos transferred	1.48±0.6	1.49±0.6	0.852
Transferred embryo			0.485
Cleavage embryo	e (e/a %)	E (E/A %)	
Blastocyst	a-e (a-e/a %)	A-E(A-E/A %)	
Clinical pregnancy rate	53.3%	39.4%	0.098*
Miscarriage rate	12.5%	37.2%	0.025*
Live birth rate	46.7%	24.8%	0.006*

*P value of univariate analysis

BMI: body mass index, AMH: Anti-Müllerian hormone, FSH: follicle-stimulating hormone