

## Response to Reviewer's Comments

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: The authors have evaluated the oxidative stress and antioxidant capacity tests as biomarkers for early detection of POI. The main idea seems to be practical but I have some critical comments. Major comment: The results of the study have demonstrated that AMH levels and AFC are different significantly between IOF and POI groups; so, the routine items could be appropriate enough to diagnose early POI. Therefore, it seems that the measurements of the studied values are not required and also extra cost for early diagnosis of POI. Minor: FSH levels for IOF and POI groups have been overlapped. Please clarify FSH cut off for categorizing the groups. Is  $10.2 \text{ mIU/mL} \leq \text{FSH} \leq 40 \text{ mIU/mL}$  for IOF group??? Is  $\text{FSH mIU/mL} \leq 10.2 \text{ mIU/mL}$  for control group???

**Reply:** Thank you for your comment. As you highlighted, the AMH level and AFC were significantly lower in the IOF group than in the control group, indicating their significance as early diagnostic markers of POI. Similarly, this study also revealed that oxidative stress is significantly higher in the IOF group before transitioning to POI than in the control group and that oxidative stress is also a biomarker for the early diagnosis of POI. It has been suggested that oxidative stress is responsible for the decrease in the number of follicles and decline in oocyte quality. Therefore, as mentioned in the Conclusion section, evaluating oxidative stress is expected to be useful not only for the early diagnosis of POI but also to enable its early treatment in the form of infertility treatment.

The IOF group had FSH levels of  $\geq 10.2 \text{ mIU/mL}$  without amenorrhea. In contrast, the POI group included women with FSH levels of  $\geq 40 \text{ mIU/mL}$  and secondary amenorrhea for  $\geq 4$  months. This information has been included in the Materials And Methods section.