Reviewer's report

Title: Effect of hypothyroidism on the hypothalamic-pituitary-ovarian axis and reproductive function of pregnant rats

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Reviewer: Amar Kumar Chandra

Reviewer's report:

In the article entitled 'Effect of hypothyroidism on the hypothalamic-pituitary-ovarian axis and reproductive function of pregnant rats' wherein hypothyroidism has been developed using propyl-thiouracil (PTU) in adult Spague Dawley female rats to investigate the differences in the occurrence of pregnancy and miscarriages after mating with male (normal?) in comparison to control using Immuno - histochemical techniques to study the expression of GnRH receptor in different hypothalamic nuclei, pituitary and ovary along with GnRH mRNA expression by qRT-PCR from those organs with the objective to understand the possible mechanism of hypothalamic-pituitary-ovarian axis regulation under the influence of thyroid hormones. Overall observations of the Reviewer are as follows

1. In this study hypothyroidism has been developed by PTU though there are several other means for doing the same. This point requires to be explained.
2. In Table 2 indicating the pregnancy and miscarriage rates is not easily understandable.
3. GnRH itself is released from hypothalamic nuclei then the reason for studying GnRHR distribution in hypothalamus requires to be explained.
4. The last line in the introduction (L 75-78) is unclear and thus these lines should be rewritten properly.
5. Vaginal plug is a standard method that is used for the occurrence of pregnancy by many workers (though there is controversy about it); there are other methods by mating the female rats during their pro-estrous phase with male followed by presence of sperm in the vagina found to be more accurate. How miscarriage rate has been evaluated should be explained clearly.
6. 'Establishment of the hypothyroid pregnant rat model' - this part is not clearly understandable (Line 108 to 125).

7. In the discussion section, line 325 - 336, a study by Lazaraus has been mentioned but its relevancy in this context is not clear.

8. In the discussion line 337-354 requires to be explained more clearly. Based on the distribution of GnRHR in hypothalamus, pituitary and ovary on immuno-histochemical analysis is a gross study without any proper labelling and on the basis of this author tried to conclude that in hypo-thyroid condition the distribution of those receptors are uneven and this is responsible for interfering the pregnancy and increasing abortion rate.

9. The paragraph (lines 354 to 360) is not clear.

10. It has been mentioned GnRH excretion in lieu of secretion in several sites. Hormones are secreted from the specific cells of the endocrine glands but is not excreted.

11. It has already been mentioned in Reference 21 that 'hypothyroidism affects the distribution of the pituitary GnRHR' (1984) then what is the novelty of this study.

12. The overall improvement in the language likely to be developed.

13. The mRNA expression of GnRHR as shown using Melt curves followed by its analysis are understandable.

The article is not suitable for publication in its present form. It requires major revision.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
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No
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Quality of written English

Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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