Reviewer’s report

Title: Metabolic alteration of urinary steroids in pre- and post-menopausal women, and men with papillary thyroid carcinoma

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Reviewer: Melpomeni Peppa

Reviewer’s report:

This paper by Man Ho Choi et al, supports that the variation in steroid levels explain the increased incidence of PTC in premenopausal compared to postmenopausal women and men. This is an interesting issue especially to scientists with closely related research interests and provides an important input on the explanation of the influence of gender differences and menopausal conditions in PTC incidence.

As the main point of the paper is the influence of steroid levels in the PTC incidence, the background knowledge and the discussion has to focus on the existing data about steroids and PTC. The receptors (Era-Erb,AR) have to be mentioned in brief as a possible pathogenetic mechanism. The main criticism is that the way the data are presented and discussed is a little chaotic and thus makes the reading and the understanding of the paper difficult.

Instead of referring to the various estrogens, androgens, corticoids, in the various studied groups, I suggest one Table with the statistically significant differences of normalized for controls values in pre-, postmenopausal women, men. The rest non significant differences or the absolute values should be described in a dense way in the Results. Also, instead of referring to various steroids it helps to categorize in power or less active estrogens and in parentheses the individual steroids) especially in the Discussion.

Try to make clear why estrogens and not androgens are responsible for the increased PTC incidence in the premenopausal women, as both are increased in this group.

Is a simple early morning urine sample enough to have accurate evaluation of excreted steroids?

It would be helpful to have the staging of the PTC. Do the observed differences in steroid levels correlate with the staging?

At which time point the patients were evaluated? Were they hypothyroid after thyroidectomy? Did they receive a suppressive dose of thyroxine and have subclinical hyperthyroidism? Does the thyroid status in terms of thyroid hormone deficiency or increased thyroxine dose bias the steroid levels, or in other words the steroid metabolism?
Did the premenopausal women receive contraceptives or the postmenopausal women estrogen replacement therapy? As you mentioned every medication has been stopped for a defined period. What is that?

In the discussion, there is no need to repeat the results and their statistical significance. This has been done in the results. The discussion has to be organized based on the results but this has to be more dense trying to discuss the main points of the paper, 1. levels of estrogens, androgens, corticoids and relationship to PTC development or progression 2. bad and good estrogens and PTC 3. possible explanations.

Discussion about the corticoids, their significance and explanations for the observed or nonobserved differences?

The conclusion is not representative of the work done.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests