Author’s response to reviews

Title: Evaluating Pre- and Post-Operation Plasma miRNAs of Papillary Thyroid Carcinoma (PTC) Patients in Comparison to Benign Nodules

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Author’s response to reviews:

Thanks for considering our paper! We revised the manuscript and worked on your suggestions, as much as possible.

Reviewer 1:

1. There are some typographical errors like miR mentioned like mir and patient information is mentioned as info. Please check and correct it for easy to understand for the readers.

Authors’ response: We revised the manuscript and corrected all typographical errors (info was corrected to information, in ‘methods and materials’ section, line 28, page 4; mir was corrected to miR in ‘Abstract’, conclusion section, page 2, line 8, in ‘Results’ section, page 12, line 15, and in ‘Discussion’ section, page 15, line 20).

2. Its better to represent the box plots for the expression of selected microRNAs using quantitative reverse transcription polymerase chain reaction rather than in a tabular form.

Authors’ response: We represented the boxplots depicting the expression levels of all evaluated miRs (Fig 1. a-d, results, page 11). Please let us know if further changes might make our graphics represent information better.

3. Why authors focussed on very limited microRNAs. Ideally it should be unbiased and through any high throughput technique.
Authors’ response: We solely evaluated these miRs since at the time of conducting this research, high throughput equipment was not available, at our research centers. However, after a long time we managed to gain access to these methods, that will use them in our future studies. It’s worthy of note that currently, couple of studies are being carried out in this regard, using these methods.

4. It will be highly appreciable if authors can provide- A, Set diagram showing miRNA expression in patients with PTC or benign thyroid nodules and healthy controls; B, scatter plot of expression of specific miRNA in the PTC and the benign nodule groups; C, scatter plot of expression of specific miRNA in the PTC and the healthy control groups.

Authors’ response: Since we evaluated two groups, our sample size was not too large, and the number of evaluated miRs were limited, providing a set diagram as well as a scatter plot does not seem too statistically correct. However, if dear reviewers have more suggestions and comments in this regard, we are fully eager to hear them.

5. The data representation is not good. Authors should provide their Q-PCR results like in Box plots of miRNA expression levels in sera of patients with PTC or benign thyroid nodules and healthy controls.

Authors’ response: We represented boxplots, depicting the expression levels of all of the evaluated miRs (Fig 1. a-d, results, page 11).

6. What is the Diagnostic value of these microRNAs. Please elaborate in discussion.

Authors’ response: We emphasized the potential role of these miRs in the diagnosis of PTC in discussion section: Page 14, line 2; Page 14, line 20, Page 15, line 22; Page 17, line 7.

7. References need to be updated with latest ones (if available).

Authors’ response: We updated the references, as much as possible. New ones include the references 12, 13, 17, 18, 19, 24, 26, 29, 31, and 32.

8. Please also elaborate your conclusion in terms of what you recommend the use of this study in future studies on large sample size.

Authors’ response: We added the following sentences in our conclusion section: “Taken together, these findings reveal the importance of miR alterations in PTC, which might value them as less invasive diagnostic tools. Our findings could be an important update for coming up with novel diagnostic for easier detection of PTC. Further studies, with larger sample size, could focus on the same miRs along with other mentioned miRs, in order to confirm or disapprove our findings in population along with determining the diagnostic cut-off for them.”

Reviewer 2:

The study is interesting and well conducted
Authors’ response: Thanks for your interest in our study.

Reviewer 3:

1. In Table 2, authors need to check the statistical significance of miR-155-5p (PTC and Control).

Authors’ response: miR-155-5p changes are significant while comparing pre- and post-operation results in PTC and control groups, separately (both P<0.001), as shown in Table 2. However, comparing PTC and control groups pre- and post-operation findings showed no significant changes as depicted in Table 3 (pre-operation comparison of two groups: P=0.61, post-operation comparison of two groups: P=0.53).

2. It is essential to measure the levels of miR221 in the plasma of PTC patients and benign controls since miR221/222 levels may provide clues for the differential diagnosis of PTC.

Authors’ response: Unfortunately, we no longer have access to our previous laboratory samples.