Author’s response to reviews

Title: Para-occupational exposure to pesticides, PON1 polymorphisms and hypothyroxinemia during the first half of pregnancy in women living in a Mexican floricultural area.

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Response to reviewers

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Reviewer reports:

Editor's comments: Please consider the further comments from the reviewers. When you produce the revised manuscript, please remember to insert the required line numbering.

Reply:

First of all, thank for your comment.

In the revised manuscript we have inserted the required line numbering. All new changes are highlighted in yellow.
Reviewer #1: Para-occupational exposure to pesticides, PON1 polymorphisms and hypothyroxinemia during the first half of pregnancy in women living in a Mexican floricultural area.

The authors have adequately addressed the raised concerns and changed the manuscript accordingly. I find that the revised manuscript has been improved, and I only have some minor suggestions:

In the revised MS, results from analyzing DAPs in urine samples from a subsample of 65 women have been included. Information on how these 65 women were selected and the number of these women categorized as para-occupational exposed or unexposed, respectively, are lacking.

In the result section, it is not apparent that the DAP results are based on a subsample and not the whole group.

Reply:

First of all, thank for your comment.

According your suggestion information about subsample selection, as well as the number of women categorized as para-occupational exposed or unexposed was included in the revised version (please see Material and Methods, pages 8-9, lines 184-186)

In the Statistical Analysis and in the Results subsections we have specified that the DAP results come from the subsample and not from the whole group (please see page 11, line 238, and page 12, lines 259-263)

Reviewer #2: The only significant observation made by this study is the association between PON1 polymorphism and hypothyroxinemia (whatever the actual reason is). This is actually stressed in the abstract.

Concerning the relationship between para-occupational exposure, OP pesticides and hypothyroxinemia, little can be concluded. The additional pesticide assays the authors made to address the reviewers criticisms are not conclusive. The differences the authors signal are not significant and far from being so.

The authors should not state "Para-occupationally exposed women had higher median urinary total DAP concentration (1.16 μmol/gr creatinine) than those who did not (0.83 μmol/gr creatinine), although this difference was not statistically significant p=0.56 " . They can only say that they found no significant difference. Therefore at this stage they can say that there is no correlation between hypothyroxinemia and para-occupational exposure in this particular study, however they cannot claim that there is no correlation between hypothyroxinemia and OP pesticides. It is quite possible that the control group in this study is also highly exposed through other pathways. This should be clearly stated by the authors.
Reply:

First of all, thanks for your comments.

According your first suggestion, We have modified the sentence "Para-occupationally exposed women had higher median urinary total DAP concentration (1.16 μmol/gr creatinine) than those who did not (0.83 μmol/gr creatinine), although this difference was not statistically significant p=0.56 " (please see Results section, page 12, lines 259-263).

Also, according your second suggestion, in the Conclusion section we have clearly stated that it is possible that the control group in this study is also highly exposed through other pathways (please see Conclusion, page 18, lines 420-423). We have also modified the conclusion in the abstract (please see Abstract, page 3, lines 56-60)

Additionally, in the Discussion section we recognize that it is possible that exposure levels of para-occupationally exposed women are quite similar to those of the rest of the study population, and that a possible non-differential measurement error along with a low variability in exposure levels among our women could explain the lack of significant association between para-occupational exposure and hypothyroxinemia (please see pages 16-17, lines 373-385).