Author's response to reviews

Title: The Association of vitamin D status and fasting glucose according to body fat mass in young healthy Thais

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Author's response to reviews: see over
Dear the BMC Endocrine Disorders Team

Thank you for your letter of October 15, 2013. We thank all reviewers for their instructive comment and suggestion.

Included please find our revised manuscripts, revised table, figure and our responses to each reviewer comments. Please note that in the revised manuscript, the changes that we have made are underlined.

We hope our revised manuscript is now appropriate to be accepted for publication in BMC Endocrine Disorders journal.

Sincerely yours,

Hataikarn Nimitphong, MD
Corresponding author
The Association of vitamin D status and fasting glucose according to body fat mass in young healthy Thais
Hataikarn Nimitphong, La-or Chailurkit, Suwannee Chanprasertyothin, Piyamitr Sritara and Boonsong Ongphiphadhanakul

We thank Reviewer I for the instructive comment and suggestion.

Responses to Reviewer I comments

Reviewer: Nansi Boghossian

Reviewer's report:
In this study, the authors examined the association between vitamin D status and fasting glucose in a group of young healthy Thais. Several issues should be addressed:

Major
  - Did the authors examine graphically the relationship between vitamin D and FPG and found that it is linear?
    
    Yes, we did as shown in the figure below. The linear regression coefficient for the relationship was 0.23, \( P < 0.001 \).

  - Did the authors test first for the significance of the interactions and based on that subsequently stratified the data? I would expect to find an interaction between gender, body fat, and FPG. What about an interaction between age and FPG? All of these should be tested first.
We have checked the statistical interactions of body fat and gender with vitamin D status on their relationship to FPG. However, no significant interaction was detected.

- Body fat x total 25(OH)D: p = 0.39
- Age x total 25(OH)D: p = 0.31
- Gender x total 25(OH)D: p = 0.95

• Line 177: The lower circulating vitamin D among obese subjects is due to the trapping of the vitamin D in the adipose tissue. This mechanism is very different from a VDR knockout mice and such an analogy between the two should not be used.

Thank you for the comment. We rewrite the sentence to “In spite of the fact that most epidemiologic studies demonstrated lower circulating vitamin D is generally associated with increased adiposity [23], underlined mechanism of the association has not been well established. Nevertheless, the mechanistic studies of this correlation in mouse model are complex. For example VDR knockout mice were lean [11]” (line 179-183).

• The argument made about the differences in the association between FPG and vitamin D based on body fat mass is not consistent. Tertile 1 showed a positive association while the 2nd tertile showed a negative association and the 3rd tertile showed a positive association again.

We agree that the association between FPG and 25(OH)D levels is not consistent across tertile of body fat mass. But we demonstrated that only the positive association between FPG and 25(OH)D of subjects in the lowest tertile of body fat was significantly found.

• Are other measures than FPG available? Fasting insulin for example? Unfortunately, we did not have other metabolic parameters such as fasting insulin, HbA1c. We added this comment to the limitation of the study (line206-208).

• What about other measures that can potentially affect both diabetes risk and vitamin D such as calcium intake for example.

We did not collect data about the calcium intake in this study. We added this comment to the limitation of the study (line210-212).

Minor
• Please provide a reference of the standardized techniques that were used in the measurements of the anthropometrics or describe the techniques briefly.

We provided the references described the techniques that were used in the measurements of the anthropometrics. (ref 17, line 94-95)

• Page 7 line 135, the wording is contradictory strong positive association although weak.

We rewrite the sentence to “it was found that there was a significant association (p=0.01), although a weak positive correlation (r=0.097)” (line 137-138).

• Since the authors measured both vitamin D2 and D3, were the results any different from the total vitamin D measurement?

Because 25(OH)D2 had a strong correlation with total 25(OH)D (r= 0.998, p<0.001) whereas 25(OH)D3 had a weak correlation with total 25(OH)D (r= 0.182, p<0.001). We further performed multiple linear regression analysis to identify the association
between FPG (the dependent variable) and 25(OH)D3 in each subgroup, stratified by gender, age group and tertile of total body fat. And all results were the same as using total 25(OH)D.

- Discussion line 145: Please elaborate on the difference between Caucasians and Asians has not been well recognized. Difference in what?
  We rewrite the sentence to “The difference of this relationship between Caucasians and Asians has not been well recognized.” (line 147-148).

- Line 188. And is likely to decrease with age. What is the reference?
  We added the reference number (ref no 26, line193).

- No references cited for lines 196-199.
  We added the reference number (ref no28, line 204).

- Tables 1 & 2 can be easily combined. Table 3 can be included as text rather than have a table on its own.
  Thank you for your suggestion. We combined table 1 and 2 and described data in table 3 as text (table 1 and line 132-133).

**Level of interest:** An article of limited interest  
**Quality of written English:** Acceptable  
**Statistical review:** Yes, and I have assessed the statistics in my report.  
**Declaration of competing interests:**  
I declare that I have no competing interests
The Association of vitamin D status and fasting glucose according to body fat mass in young healthy Thais
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We thank Reviewer I for the instructive comment and suggestion.

Responses to Reviewer II comments

Reviewer's report
Title: The Association of vitamin D status and fasting glucose according to body fat mass in young healthy Thais.
Version: 1 Date: 25 September 2013
Reviewer: Michael Holick

Reviewer's report:
1. The authors have nicely documented vitamin D status in a working environment in Thailand demonstrating significant vitamin D deficiency. It is however unclear how meaningful the conclusion is regarding vitamin D status and fasting blood glucose levels since there was a positive association only in the group that had the lowest 25-hydroxyvitamin D levels. This could be simply a statistical fluke rather than being physiologically meaningful.

   • Were these blood samples taken at the same time of the year? Was there a seasonal variation in 25-hydroxyvitamin D levels and more importantly fasting blood glucose levels?

   Yes, these blood samples were drawn at the same time of the year. Therefore, a seasonal variation in 25(OH)D levels should not be concerned in this study. Nevertheless, we previously reported that mean 25(OH)D level from blood samples obtained in the rainy season was the lowest and was significantly different from those collected in winter and summer[1]. There is no report about seasonal variation in FPG levels in Thai.

2. There is a wide range for BMI. Since the authors have a relatively large number of subjects it would be of interest to plot BMI with 25-hydroxyvitamin D and fasting blood glucose.

   Thank you for your suggestion. Scatter plots of FPG vs. total 25(OH)D according to body fat mass tertiles have been added in figure in the manuscript, as shown as the following.
Figure Scatter plots of fasting plasma glucose and total 25(OH)D according to body fat mass tertiles.

The 1\textsuperscript{st} tertile (n=674)

The 2\textsuperscript{nd} tertile (n=664)

The 3\textsuperscript{rd} tertile (n=652)
3. It is doubtful that this study is contrary to most studies regarding vitamin D status and diabetes since having a higher fasting blood glucose in the normal range is not necessarily related to increased risk for type 2 diabetes. We agreed with this comment as we discussed in the discussion part (line 198-199).

- This needs further explanation.

The mechanistic underlined this finding is beyond the scope of our study. We could only hypothesized that these relatively young population (mean age of 40 years) might have higher amount of brown adipose tissue. Then vitamin D may have a greater influence in inhibiting the function of brown adipose tissue rather than in inhibiting lipogenesis and its metabolic consequences in white adipose tissue (line 193-196).

- Did the authors observe higher blood sugar levels in subjects who had metabolic syndrome or type 2 diabetes? Were they excluded from this study? Unfortunately, we did not have data about previous history of diabetes or measurements for metabolic syndrome in our subjects. We added this limitation in our discussion part. Nonetheless, statistical analysis which including or excluding subjects who had FPG ≥ 7 mmol/L (126mg/dL) provided the same results (line 208-210).

Level of interest: An article of importance in its field

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

Reference