

Peer Review File

Article Information: <http://dx.doi.org/10.21037/atm-20-5203>

Reviewer A

Authors reported well written and well-balanced paper in which the role of FGF-11 in T1DM population was evaluated. The main results of the study were "Low serum FGF19 level is associated with T1DM, which could serve as a risk factor for T1DM". The design of the study was cross-sectional study. The methods were described well, the results sounded impressive, the discussion was written accurate and decisive. However, there some items need to be explained.

1. Study design should be reported as flow chart with clear criteria for inclusion and non-inclusion.

Reply 1: Thank you very much for your comments. We agree with you that the inclusion and exclusion criteria need to be clearly stated.

Changes in the text: Based on your suggestions, flow charts containing the inclusion and exclusion criteria were added as Figure 1 in the main text. In addition, we added a detailed description of the inclusion criteria to the Method section (Line 75-79).

2. Sample size calculation: please, add a calculation with appropriate formula.

Reply 2: We appreciate your constructive comments.

Changes in the text: According to your suggestion, we added a sample size calculation and related formula to the method section (Line 111-118).

3. The duration of the T1DM was not evaluated, while there are numerous studies which were reported the association between CV biomarkers and duration of T1DM, but not for T2DM. Please, check and explain.

Reply 3: Thank you very much for your suggestions.

Changes in the text: According to your suggestions, we added duration of T1D in Table 1. Then we investigated the correlation between duration of T1D and FGF19 in Table 2. There was no significant correlation between serum FGF19 levels and duration of T1D (Line 144-145).

3. The issue "low levels of FGF-11 predicts T1DM" is not supported by the results of the study and it is an assumption only. Please, make the sentence a little bit less causative adding possibilities, but not decisive fact.

Reply 3: Thank you very much for your comments. We truly agree with you that this study cannot explain a causative results between FGF19 levels and T1D as it is a cross-sectional study. We also mentioned this in limitation part of the Discussion section (Line 234-237).

Reviewer B

In this study, circulating levels of FGF19 were determined in patients with type 1 diabetes (T1D). The manuscript is well described and based on its results the authors suggest that FGF19 may be considered as a risk marker for T1DM.

I only have two concerns regarding the FGF19 method of quantification

1. How long were the samples stored and under what conditions? Since it is mentioned that the patients were recruited between 1999 and 2010. Were the controls also recruited at the same time? Please describe this point in more detail.

Reply 1: Thank you very much for your comments. The collected serum samples were stored in -80 degree freezers from 1999 to 2010 for ELISA measurement, and avoided thawing. We compared the serum FGF19 levels between T1D samples collected before year 2005 and in 2005 (N = 41) and those collected after 2005 (N = 40), and found that there was no obvious difference in FGF19 levels between the two groups ($P > 0.05$). Healthy controls were also collected at the same time. And we have mentioned this in Method Section as you suggested. Changes in the text: Line 85.

2. What quality control was used for the ELISA's? i.e. were the samples measured in duplicate? What was the coefficient of variation?

Reply 2: Thank you for your comments. According to the manufacturer's instructions of the ELISA kit, we used high- and low- quality controls provided by the kit. In the preliminary experiments, we measured 10 samples in duplicate and found the variation of the duplicated same sample was less than 5%. Thus, the formal experiments were not done in duplicate. The intra- and interassay coefficients of variation were 6.0% and 7.5%.

Changes in the text: We revised the measurement of ELISA in the Method section, with the revised places marked in red (Line 109-110).