Reviewer's report

Title: Prevalence of Non-Alcoholic Fatty Pancreas Disease (NAFPD) and Its Risk Factors among Adult Medical Check-Up Patients in a Private Hospital: A Large Cross Sectional Study

Version: 3
Date: 21 September 2015
Reviewer: Gabor Firneisz

Reviewer's report:

In general the manuscript improved, yet there are still specific points that – in my view – still should be further discussed and improved before publication and these very short replies may be inappropriate at some points.

Specifically:

Q No 11:
“Isn’t Beta-cell lipotoxicity and subsequent Beta-cell dysfunction important from the point of diabetes mellitus when there is an excessive ectopic fat deposition also in the pancreas? Why do authors only mention insulin resistance, when the association between diabetes mellitus and NAFPD is discussed?”

A: “Because it is the available predominant theory.”

In contrast, adipose cells infiltrating the pancreas in non-alcoholic pancreatic disease are – especially recently - in the focus of interest due to their close contact to Langerhans islets in the human pancreas that may be fundamentally important in the development of Beta-cell dysfunction (see question – also refer to the 47th Claude Bernard Lecture by Prof. Hans-Ulrich Haering titled “Understanding phenotypes of prediabetes: essential to influencing progression to type 2 diabetes” at EASD annual meeting 2015)

Therefore I would still suggest not only to mention the equally dominant and important B-cell dysfunction but rather also to address and discuss this in an appropriate way in the manuscript.

Q No 6:
“Despite that 62 patients with diabetes mellitus (I assume type 2, but please clearly indicate it) participated in the study there is a complete lack of data on their drug use. Specifically PPARg agonist, statin, DPP-4 inhibitor and GLP-1 analouge/mimetic drug use and its relation to NAFPD would be interesting (and possibly metformin also, yet we do know that metformin fails to upregulate adipokine hormone levels therefore not specifically beneficial in NAFLD). So please include drug use in the analysis.

A: “This study is not aimed to see the medication as independent risk factor but more in the metabolic factors.”

There are a number of observations they made that may not be taken out from
the clinical situation of drug use: ie. authors state that higher than 100mg/dL fasting blood glucose levels (or plasma? – still unclear in the revised form) were associated with NAFLD.

They also report that type 2 diabetes has been a significantly associated with NAFPD (OR:1.95, p<0.001) , but they could not confirm it in their multivariate analysis. Reporting any result in such a way, itself is somewhat confusing, instead authors suggested that “type 2 diabetes is a confounding factor”.

To further clarify this I still suggest to complete lack of data on their drug use. This is due to that the drugs typically used by individuals both have an effect on the metabolic factors (i.e. fasting glucose levels, etc) they analyze and also on the outcomes they try to associate their results to (i.e. GLP-1 receptor agonists, possibly DPP-4 inhibitors and confirmedly also pioglitazone have an effect on the intrahepatic lipid content – clinically on NAFLD (and potentially on NAFPD?)). Without the analysis of the drug use data their results may be confounding even on their main outcomes and their main observations.

Q No 7:
“How was the lack of having diabetes mellitus diagnosed?........”

A: “This is MCU setting as our hospital MCU standard examination to diagnose DM”

This answer is still not clear for the reviewer – did those individuals who were in non-diabetic study group undergo:
- a 75g CH OGTT
- or HbA1c was measured
- or both (as these two tests do not entirely identify the same population with diabetes)

to assess the presence diabetes mellitus?
- or the lack of diabetes, so the non-diabetic study group in their analysis was only established on patient history and drug use?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests