

Reviewer #1:

Specific Comments to Authors:

1. I suggest: The authors should investigate the risk reported in the literature between pancreatic cancers and non-alcoholic fatty pancreas disease. Which may be the pathophysiological mechanisms that determine it.

Response: A new paragraph has been added addressing the issue (Page 6, Line 179).

2. They should also highlight the diagnostic difficulty of the diagnosis of non-alcoholic fatty pancreas disease, both from the serological point of view (often it is not associated with an increase in pancreatic enzymes) and instrumental, and how CT and MRI or MR spectroscopy (MRS) are not very usable investigations as screening. The authors should describe that the sensitivity of the ultrasound is low.

Response: As correctly pointed out NAFLD is usually not associated with increase in pancreatic enzymes and various non-invasive imaging modalities are often used in clinical and research setting. The various imaging modalities playing important role in diagnosing NAFLD are detailed in the text (Page 4, Section 3).

3. Bibliography does not respect the indications of the journal.

Response: The bibliography has been modified as per journal style. Additionally more references, including a few recent references have been added in the manuscript.

Reviewer #2:

Specific Comments to Authors: This is a review article regarding the association between pancreas fat and type 2 diabetes. The review was written concisely but rather superficially. There are some comments.

1. There are discrepancies between the Epidemiology section and Pathophysiology section: The authors stated that “the prevalence of pancreatic steatosis was independent of age and sex” in Epidemiology but that “age and male sex are other risk factors for NAFLD” in Pathophysiology. The authors also stated that “BMI and waist circumference did not have any association with pancreas fat” in Epidemiology but that “obesity has been implicated as the most important risk factors for NAFLD” in Pathophysiology.

Response: In the epidemiology section we mentioned about a meta-analysis (Singh RG, Metabolism. 2017) where the authors observed that pancreatic steatosis was

independent of age, sex and BMI. Of note, 9 of 11 studies included in this meta-analysis were conducted in Asian populations, thereby raising questions regarding the generalizability of the data. More studies in different ethnic populations, especially those with high rates of obesity and metabolic syndrome, would be valuable in delineating the true association of pancreatic steatosis. In the pathophysiology section we have described some of the risk factors which have been found to be associated with NAFLD in various studies which also include obesity, age and male sex. Hence there are certain discrepancies existing in the literature itself. However, as the description in the epidemiology section has created some confusion in the mind of the reviewer, we have modified line no 104-106 in page no 4.

2. There are cons and pros on the causal role of pancreas fat on type 2 diabetes. Studies in section 4 should be summarized in a table. 3.

Response: Studies showing association and lack of association of pancreatic fat with type 2 diabetes in section 4 have now been summarized in table. 2.

3. There are a number of previous reviews on this topic. The authors should state the novelty of this review in the manuscript.

Response: The reviewer has correctly pointed out that there are a number of previous reviews on this topic; however, uncertainty still exists. The association between T2D and NAFLD is controversial. Some studies reported more pancreatic fat accumulation in T2D subjects than those without diabetes, while others observed no difference (Page 4, line 87-89). Here, on the basis of comparison of various studies, we propose that pancreatic fat is an important contributor in the pathogenesis of T2D.

4. The search criteria is unclear. A flow chart of literature selection should be presented.

Response: Since the article is in the form of a mini-review and not a systematic review. Hence, we did not include the search criteria.