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LETTER TO THE EDITOR

Relationship between soluble transferrin receptor and type 2 diabetes mellitus: A meta-analysis

I read with interest the article titled "Iron metabolism and type 2 diabetes mellitus: A meta-analysis and systematic review" by Liu *et al.*[1] published in this journal. Noteworthy is the intent of the authors to show, as far as possible, the effect of different levels of each iron biomarker on the risk of type 2 diabetes mellitus. Nevertheless, there are several issues that are worth addressing.

First, the authors included, in the meta-analysis on the relationship between soluble transferrin receptor (sTfR) and type 2 diabetes mellitus, the result obtained in a group of non-obese participants, but not that observed in obese participants, both reported in the same publication by our research group[2]. Second, the results found by Rajpathak *et al.*[3] in obese individuals were not included in this meta-analysis, but were included in the meta-analysis on the relationship between ferritin and type 2 diabetes mellitus. Third, another publication of our research group, also within the PREvención con DIeta MEDiterránea study, compared the lowest concentrations of sTfR with the highest concentrations, as

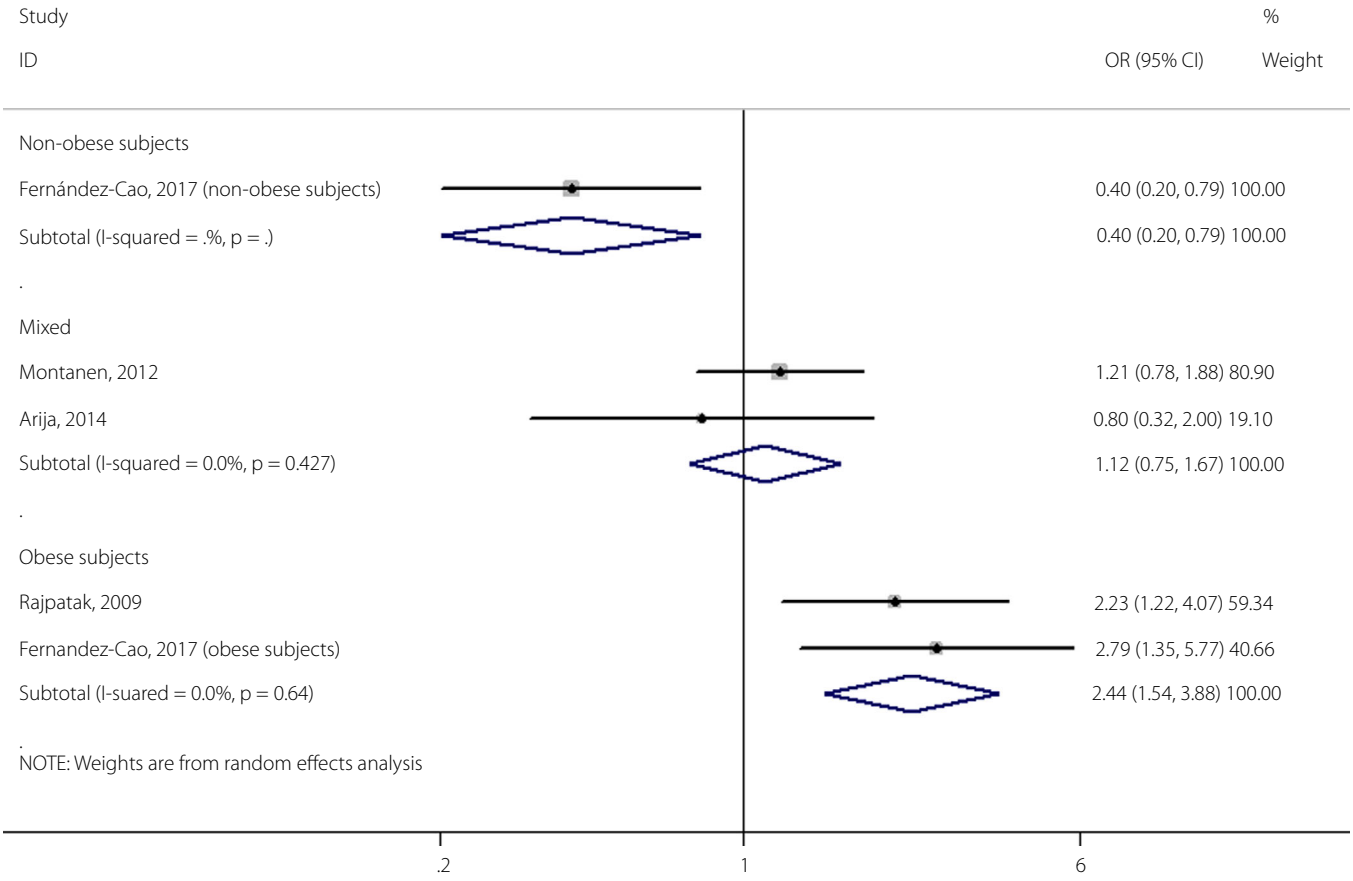

Figure 1 | Forest plot of the pooled effect size of the highest versus lowest soluble transferrin receptor for type 2 diabetes mellitus according to obesity (non-obese, mixed and obese participants). Squares represent odds ratios for each study, and the size of the square is the study-specific statistical weight. Horizontal lines show the 95% confidence interval (CI) of each study. The diamond represents the odds ratio estimate with corresponding 95% CI. OR, odds ratio.

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the reference category[4]. Nevertheless, other included studies in this meta-analysis carried out the analysis using the lowest quantile as the reference category[2,3]. This fact might be a significant threat to the validity of the results. The situation is similar for the meta-analysis on the relationship between the sTfR : ferritin ratio and type 2 diabetes mellitus. Finally, the two results of our group, included in the meta-analysis, were obtained from samples with participants in common[2,4]. Therefore, besides the scarce number of publications included in this meta-analysis, an inappropriate weight was given to the data, which might introduce bias and unreliable results.

In our previous study, we observed an interaction of obesity on the relationship between sTfR and type 2 diabetes mellitus[2]. To verify the influence of obesity on this association, a stratified meta-analysis, based on whether the sample was of obese participants, non-obese participants or both at the same time (mixed) was carried out, including the same studies selected by Liu *et al.*[1] A random effects model and the generic inverse variance method were used to calculate the pooled effect size, reported as the odds ratio and 95% confidence interval. The forest plot (Figure 1) showed an inverse and a direct association between sTfR and type 2 diabetes mellitus in non-obese subjects and obese subjects, respectively. When samples were formed by obese and non-obese subjects together, a non-significant association was observed. Interestingly, undetectable heterogeneity was found in subgroups (I^2 = 0.0%). As we observed in our study[2], obesity might play a role in the association between sTfR and type 2 diabetes mellitus. Further research is warranted to elucidate the influence of obesity on this relationship, as well as the underlying potential mechanism.

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DISCLOSURE

The author declares no conflict of interest.

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