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Authors' response

We thank Dr Andrade and colleagues for their interest in our study[1]. Whereas critical assessment of any study is important for the overall betterment of scientific community, we would like to differ to the authors in some of the concerns raised.

The major concern was the lack of a defined primary outcome in the study. We would like to point out that our findings were the part of a genome-wide association study of childhood obesity and related traits in Indians, as clearly mentioned in the experimental section of the manuscript[1]. This was a study of cross-sectional design in a large group of Indian adolescents (n=4438). We could observe some distinct patterns in the anthropometric indices and inflammatory profile of adolescents from private and government funded schools, which prompted us to venture for a thorough analysis. As mentioned in the manuscript, our study was aimed to compare the inflammatory state in urban Indian adolescents of private and government-funded schools in New Delhi, India, belonging to two different socio-economic strata, with differing obesity status, gender and age.

Another question was about the relevance of including analysis for sub-groups of extremely lean and obese study participants in the study. This part of the study, as appropriately suggested by one of the reviewers, was to explore the inflammatory trends in morbid conditions of lean and obese study participants. This is important as extreme BMI conditions can bring a drastic outcome in terms of inflammatory state of adolescents[2]. We have not tested any parameter for association in these sub-groups, rather all participants of the aforementioned groups were evaluated for distribution (medians with inter-quartile range) of anthropometric indices and different inflammatory markers, also after stratification by gender and age[1].

Furthermore, there was a question raised on the lack of Type 1 error risk assessment for multiple linear regression analysis. We agree that we did not employ tests like Bonferroni or Hochberg correction to test for false positives. However, we would like to bring to the attention that almost all of our findings were significant with a P value of <0.001. Some of these P values were extremely small and we did not report the exact P values in many cases. Needless to say, that most of the tests would hence numerically be significant even if we apply the most stringent of multiple testing, without inflating the Type-1 error (if the authors are satisfied with a 5% or 1% Type-1 error). Moreover, in the discourse of Type-I error, it should always be kept in consideration, that not all the variables studied here were independent of each other. There is a great deal of dependence in obesity related variables; as has been shown both epidemiologically and in many cases, scientists have worked out unified biological network and pathways simultaneously affecting many of these. It is, therefore, not a set of independent statistical tests to apply the standard multiple testing problem; nor is the inflation of the Type-I error a huge problem as we are in some way trying to capture the different aspects of metabolic disease. The philosophical debate of our over-emphasis of P value in scientific research is important, and fiercely debated. This response is not to reopen that debate all over again. We would like to emphasize on the common denominator in the debate, where almost everybody agrees: "statistical significance does not automatically imply clinical importance". We think our results, emphatically show that the set of biochemical parameters, which is a metric of metabolic health, shows huge difference in the cross-classified group of adolescents whom we have studied in great detail.

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