Professor Timothy R Koch

Editor-in-chief

World Journal of Diabetes


**Dear Prof. Koch**

Greetings;

Thank you very much for your letter informing us of your decision and the reviewer comments regarding the manuscript **47300,** entitled **"A prospective study of total and various types of vegetables and the risk of metabolic syndrome among children and adolescences".** The manuscript has been revised according to the referee' comments. Herewith attached the revision of manuscript as well as a point by point response (R) to the reviewers' comments (C).

**Yours sincerely,**

**Somayeh Hosseinpour-Niazi**

Nutrition and Endocrine Research center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

**Response to specific comments to authors**

*The study investigates the relationship between consumption of vegetables and the risk of metabolic syndrome among children and adolescences. The results sound interesting and having valuable data. However, some of the manuscript should be improved before the consideration of acceptance for the Journal.*

R. Thank you for the constructive comments and the opportunity to revise our manuscript.

**Major comments:**

*C1. In this study, individuals with MetS were excluded at baseline. However, I would like to know about the participants with pre-MetS or those having impaired components of MetS. In Table 1, component of MetS, for instance, systolic blood pressure, FPG, HDL-C (lower) were significantly higher in the group of lowest vegetables consumption.*

R. Considering that the aim of this study was to investigate the association between various types of vegetables and MetS, we excluded subjects with MetS, but participants with pre-MetS or less than 2 components were not excluded from study. Based on suggestion, the prevalence of Pre-MetS (having two components) and subjects with zero or one component of MetS at baseline has been reported in Table 1 and on page 10 as follows "==Pre-MetS has been defined as having two components of these criteria==" and on page 12 as follows "==The prevalence of subjects with 0, 1 and 2 components of MetS did not differ across quartiles of vegetable consumption.==".

*C2. In Table 3, are parameters adjusted for MetS baseline parameters or those 3.6 years later?*

*Please add the description of baseline parameters or 3.6 years later.*

R. Agreed and done as suggested in Table 3 and on page 11 as follows: "*Model 2 was adjusted for age, gender, physical activity, family history of diabetes, total energy- and cholesterol intake at baseline. Model 3 was additionally adjusted for BMI at baseline.*"

*C3. Taken together, these issues may contribute to the causality. It is possible that individuals with MetS or pre-MetS predispose to consume less amount of vegetables especially allium and green leafy vegetables, which may be a bystander but not a cause for MetS. Therefore, it may be better to add explanations about the possibility.*

R. Agreed and added on page 11 as follows "*By multivariable regression models, we further performed stratified analysis by categories of number of components of MetS (0, 1 or 2 components of Mets) at baseline to estimate ORs of MetS based intake of total and various types of vegetable consumption (above/below the medians).*" and page 12 as follows: "*There was no significant difference in total vegetable consumption (median (IQR)) between participants with 0 (206 (145-322 g/day)), 1 (217 (144-351 g/day)), and 2 component of MetS (226 (161-345 g/day)) at baseline.*"

Also on page 13 as follows "*Table 4 presents ORs for MetS based intake of total and various types of vegetable consumption (above/below the medians) among participants with 0, 1 or 2 components of MetS at baseline. Among participants with 1 component of MetS, green leafy- and allium vegetables reducer risk of MetS by 71% (0.23, 95% CI: 0.07-0.71) and 77% (0.29, 95% CI: 0.07-0.71), after adjustment for confounding factors. No association was found between total-, fruity-, root-, stalk-, potatoes, starchy-, and cabbage vegetables and risk of MetS among participant with*

≥ 2 component at baseline. " and "*In addition, we found that among participants with 1 components of MetS, consumption of allium- and green leafy vegetables reduce risk of Mets. However limited sample size in participants with 0 and 2 component of MetS may influence the association between consumption of vegetables and MetS.*"

*C3. I wonder that the criteria for MetS can differ between child aged 6 yo and adolescent aged 18 yo. Can you divided participants into, for instance, two groups, younger than 10 and older than 9 yo.*

R. Definition of MetS according to different age groups differ among children and adolescents, e.g the definition of MetS by International Diabetes Foundation differs among children and adolescents in 10-16 year- and >16 year- olds, no definition has been given for children <10 years (*Al-Hamad D & Raman V. Metabolic syndrome in children and adolescents. Transl Pediatr. 2017 Oct; 6(4): 397–407*). According to the Cook et al study, "*closest representative values obtainable from pediatric reference data determine criteria of MetS among children or adolescents Using Third National Health and Nutrition Examination Survey for definition of MetS*". Therefore we used this criteria for definition of MetS among children and adolescents in the current study. However SBP/DBP- and WC percentiles (for sex, age) have been determined until the age of 18 years, and during follow-up, some adolescent participants (≥ 16 years) had reached the age ≥18 years; therefore the components of MetS (regarding no percentile of DBP/SBP or WC for these age group) were determined according to the Joint Interim Statement of the International Diabetes Federation that define the MetS for adults (aged ≥ 18 years). This approach was used in other prospective studies given below:

- Lin WT et al. Clustering of Metabolic Risk Components and Associated Lifestyle Factors: A Nationwide Adolescent Study in Taiwan. Nutrients. 2019 Mar 9;11(3).

- Li G et al. Childhood retinol-binding protein 4 (RBP4) levels predicting the 10-year risk of insulin resistance and metabolic syndrome: the BCAMS study. Cardiovasc Diabetol. 2018 May 14;17(1):69.

- Hooshmand F et al. Modified Healthy Eating Index and Incidence of Metabolic Syndrome in Children and Adolescents: Tehran Lipid and Glucose Study. J Pediatr. 2018 Jun;197:134-139.

- Asghari G, et al. Dietary Approaches to Stop Hypertension (DASH) Dietary Pattern Is Associated with Reduced Incidence of Metabolic Syndrome in Children and Adolescents. J Pediatr. 2016;174:178-184.

*C4. Other factors including education and incomes are likely to interact the outcomes because dairy consumption substantially differs among quartiles.*

R. Considering that the current study, participants were selected among residents of Tehran's urban district 13, the socioeconomic status did not differ among participants. However based on reviewer' suggestion, we reported education and occupational variables for parents in Table 1 and on page 12 as follows "*No statistically significant associations were found for age, gender, physical activity levels, family history of diabetes, parental education level and occupational status and BMI.* "

**Minor comments**

*C5. In the Table 1, metabolic syndrome should be described as After 3.6 y MetS.*

R: Agreed and corrected as suggested.


*C6. In the Table 1, serum triglyceride should be described as median (interquartile ranges) because of large SE.*

R: Agreed and corrected as suggested in Table 1 and the statistical analysis section as follows "*data are presented as means ± SE and ==median (interquartile range)== for continuous variables*" (Page 11)