Author's response to reviews

Title: Metabolic syndrome in a cohort of Chinese schoolchildren: prevalence and factor analysis

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Author's response to reviews: see over
Dear editor,

Thank you for giving us the opportunity to revise and re-submit our manuscript. We have carefully read the critiques from the reviewers and incorporated their comments into the text. I hope this improved manuscript will meet the high quality of your journal and be published timely.

Here is a breakdown of the modifications we did according to reviews specific comments

**Reply to prof. Punithavathi Narayanan:**

The original comments:

1. Is the question posed by the authors well defined? The title says that the study is examining the prevalence using different definitions and factor analysis. But the objective is not in line with the title stating that it wants to examine the role of adipokines in the clustering metabolic risk factors.’ The difference in prevalence using different criteria is to be expected. So the purpose of this paper is not very clear since it does not state that one criteria is better than the other in predicting future cardiovascular morbidity or further progression of the syndrome.

Thanks for your interest on our work. Actually, there are two major purposes as the paper title has been shown:

Firstly, since there is no general consensus exists regarding the definition of MS in children and adolescents, we want to compare the different prevalence of MS in Chinese children based on the two commonly used definitions of pediatric MS. Our study will be helpful to clarify which criteria will be more valuable for predicting further progression of the syndrome or future cardiovascular morbidity after our undergoing follow-up study, and we believe the data from this large sample of Chinese children will be helpful to perfect the diagnose criteria of MS.

Second, we want to determine the clustering pattern of MS in children by factor analysis. Recently, a number of other factors besides those traditionally used to define MS that are also linked to the syndrome have been identified; considering the important role of adipocytokines in the pathogenesis of MetS, we particularly examine the role of leptin and adiponectin as additional component in the clustering of metabolic risk factors. We want to explore which condition contributes larger to the pathogenesis of MS.
2. Though they acknowledge that IDF suggests that MS as entity is not diagnosed below the age of 10 years it is not clear why the authors included that age group. Despite the IDF group recently proposed a new pediatric definition of MS, no general consensus exists regarding the definition of MS in children and adolescents at present. Different regions or groups are still exploring the pediatric MS criteria to fit their racial characteristics. Furthermore, studies published so far have used their own set of variables, number of criteria and different cut-off points to define risk factors associated with MS. IDF does not recommend diagnosing MS for children under 10 yrs, but still emphasize to pay high attention to the children with risk factors of MS. So, in our study, we used the two commonly used definitions: the IDF criteria and the modified ATP-III standard, to evaluate MS incidence in children under 10 yrs old, and still found high ratio of risk factors of MS in this age group. So, we want to emphasize that MS in children under 10 yrs is worth of concern. Hence, the existing proposed MS definition should be extended to include children below ten years old.

3. Obesity could have been defined using IDF cut off points instead of one recommended by Working group on obesity in China. That will be helpful while making comparisons across regions and during meta-analysis.

Our study is a 15-year follow-up study. The screening obese children at baseline was initially according to the standards of China Obesity Task Group, so it seems not so necessary for our cohort study to re-evaluate obesity based on the IDF standard. However, data can be provided if needed in the future meta-analysis.

4. They conclude that ‘Leptin/adiponectin was strongly associated with central obesity, and may be taken as a possible component in MS.” Central obesity is an easy measurement which can be carried out in the field and it is not clear how adding Leptin/adiponectin will improve the definition of MetS?

The currently used traditional components of MS are really simple for practice, such as central obesity, easily assessed using waist circumference. However, epidemiical studies have been demonstrated that predictive power of the CVD risk based on current definitions of MS in adult is not very outstanding; this also is the point of contention about necessity of MS diagnosis. So the IDF consensus group has highlighted a number of other parameters that appear to be related to the MS,
which should be included in research studies to help determine the predictive power of these extra criteria for CVD and/or diabetes. The use of these additional factors in research will also allow further modification of the definition if necessary and the validation of the new clinical definition in different ethnic groups. On the other hand, as we know, not all the obesity suffers from metabolic disturbances, a subset of obese individuals are called “metabolically healthy but obese” phenotype; thus, obesity consists of different subtypes with different metabolic profiles. As the directly reflection of endocrine function, serum adipokines profiles may be more informative and accurate than BMI or WC to identify individuals with high-risk of MS, especially to identify metabolic healthy but obesity phenotype. Moreover, because of their critical roles in MS, adiponectin, leptin, especially their ratio have been suggested to be useful serum markers for diagnosis of MS in previous studies. We believe that based on our large sample, after finish our follow-up study, we can provide further more informative results.

5. Though English is probably not the first language of the authors the manuscript has many grammatical errors that are distracting to the reader.

We have sought the assistance of a fluent English speaking colleague and a professional editing service to correct our manuscript.

Reply to prof. Constantina Papoutsakis,

Original comments:

1. This paper compares the prevalence of MS using 2 definitions: IDF and modified ATPIII and employs factor analysis to identify the features that play the biggest role in the MS. The quality of the writing requires significant improvement. Grammar and syntax should be reviewed by a native English speaker who is familiar with the demands of writing a paper in English for a medical journal. Also, there are numerous spelling errors in the manuscript and Tables. Having said that, the basic aim of the study is of high scientific interest. The authors should be commended for their advanced statistical analysis and should be given the opportunity to revise their written work. Thanks for your kind comments.

2. Consider revising the title to reflect the outcomes of the factor analysis which are most
interesting. The paper did not use different definitions of the MS, it only used 2. Given that the IDF requires that the central obesity criterion is met, it is already a given that the IDF definition will always produce a much lesser prevalence, so this is not really worth emphasizing a whole lot in the title or in the paper itself.

We already do some changes.

3. Several papers have been published on metabolic syndrome and adipokines in children. Authors of this paper should discuss similarities and discrepancies with available data in theirs discussion. For example, it has been suggested that associations between metabolic syndrome and adipokines in the age range of subjects of this paper are confounded by pubertal changes. This needs to be discussed. It is not obvious how the authors controlled for Tanner in their analysis. This should be explained in their methods in more detail.

Sex is the most important influence factor of leptin and adiponectin levels, so our statistics analysis using correlation and factor analysis was both stratified by gender. However, we found that puberty had only a mineral effect on the association of adipokine leptin and adiponectin with metabolic syndrome, and it might be due to large sample size. So, because of negative result and limited space, we didn’t list the statistical results stratified by pubertal stage.

4. The authors suggest adding the adiponectin/leptin ratio as one more feature of the MS in children. It is not clear why adiponectin/leptin ratio or either one on its own would be of added value. If a high WC identifies children at risk for MS, why measure adiponectin and or leptin? What is the scientific value? The authors should explain this in the discussion.

Actually, the currently used traditional components of MS are really simple for practice, such as central obesity, easily assessed using waist circumference. However, epidemiological studies have been demonstrated that predictive power of the CVD risk by using current definitions of MS in adult is not very outstanding; So the IDF consensus group has highlighted a number of other parameters that appear to be related to the MS, which should be included in research studies to help determine the predictive power of these extra criteria for CVD and/or diabetes. The use of these additional factors in research will also allow further modification of the definition if necessary and the validation of the new clinical definition in different ethnic groups. On the other hand, as we know, not all the obesity suffered from metabolic disturbances, a subset of obese individuals are called “metabolically healthy but obese
phenotype”; thus, obesity consists of different subtypes with different metabolic profiles. As the directly reflection of endocrine function, serum adipokines profiles may be served as a more valuable tool than BMI or WC to identify individuals with high-risk of MS, especially to distinguish the metabolically ‘healthy’ from ‘unhealthy’ obese phenotype. Moreover, because of their critical roles in MS, adiponectin, leptin, especially their ratio have been suggested to be useful serum markers for diagnosis of MS in previous studies. So, we believe that based on our cross-sectional analysis with large sample size, after finishing the next follow-up study, we can provide further more informative evidence about the adding value of adiponectin/leptin ratio as one more feature of the MS in children.

5. The authors state in the discussion: #childhood MS should be considered a disease entity#. In general, there has been some recent controverseries about the term "Metabolic syndrome" (Diabetologia, March 2010). Thus, the reviewer suggests that the authors address this matter in the manuscript.

Thanks for your kind comments.

Abstract.

Rewrite results of abstract. Confusing as written. It should be written in a way so that even when someone is not an expert in factor analysis can understand the essential findings that come out of the factor analysis. Also, report specific prevalence of each MS factor according to IDF.

We already do change.

Intro: contains several spelling errors. Include some basic literature on adipokines and MS in children to support the aim of your study.

Methods: Include citations for Tanner stage assessment. Be specific. How was this done? By pediatrician? Or by showing visuals or how? As stated in Methods, features of the MS were explored according to the International Diabetes Federation (IDF). Thus, the authors ought to include a detailed description of the IDF definition, and specifically th authors applied it (in addition to the citation that is already in the paper).

We have done some changes and supplement.

Statistical analysis: It is not clear what adjustments took place for confounding
factors if any. For example, was the analysis adjusted for Tanner status?
Provide citations and a more detailed description for the PCA specifically.
We had performed the correlation and factor analysis stratified by gender and puberty.
But we found puberty had mineral effect on the results of factor analysis, due to the limited space, we didn’t list all those results in the article.

Result's section: The reviewer suggests to present only the appropriate results. Consider to focus only on results from children that are older than 10. This would be consistent with what is recommended. The number of Tables is excessive. Is there a way to reduce the number of Tables?
Thanks for you kind suggestion, we have already done changes.