

Non-traditional biomarkers of eating disorders symptoms among female college students

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Handling editor:

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1st editorial decision

Date: 8 aug 2016

Ref.: Ms. No. JCTRes-D-16-00020

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Journal of Clinical and Translational Research

Dear Mrs. Lofrano-Prado,

Reviewers have now commented on your paper. You will see that they are advising that you
revise your manuscript. If you are prepared to undertake the work required, I would be pleased
to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you resubmit your work.

Your revision is due by Sep 07, 2016.

To submit a revision, go to <http://jctres.edmgr.com/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Rowan van Golen

Associate Editor

Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The manuscript examines potential diagnostic tools for eating disorders in a cross sectional study. The manuscript could contribute to the body of knowledge in this content area if multiple issues are addressed prior to publication. A major flaw of the study is the lack of adjustment for BMI and previous diagnosis of eating disorders.

Abstract

- The "Background" and "Relevance to Patients" does not recognize the cross-sectional nature of the study, causality cannot be determined and therefore assumptions of the utility of these biomarkers as early diagnostic tools cannot be establish. Please review background to include probable utility of biomarkers when used with diagnostic questionnaires.

Introduction

- Please review the references for this statement: "health sciences students are more vulnerable to develop ED relative to other specialties", the references are cross-sectional studies that do not determine if health science students are more vulnerable to ED or if patients with ED are more likely to attend health science studies.

Methods:

- It is not clear whether subjects with chronic diseases such as Rheumatoid Arthritis were excluded, and if subjects did intense exercise before that blood draw that could increase acute reactants as the ones tested.
- Obese subjects have also been found to have increase reactants, please further discussed if BMI was taking into consideration for the inclusion or exclusion of this study.
- Please clarify if subjects with previous diagnoses or in treatment for ED were identified since this subjects could have screening tests negative but positive biomarkers or viceversa.

Results/Discussion:

- It would be interesting to know if the demographics of the subjects that refused blood work was different from the participants that consented.
- Utility of regression models is questionable when BMI and previous diagnosis of ED is not taking into account. Controlling for obesity-known to have increase markers could also be relevant.
- It would also be important to address if these biomarkers have a correlation with the severity of the scores.

Reviewer #2: This paper describes the correlation between biomarkers and ED symptoms as

assessed by established scales. Results are in line with previous suggested findings also confirmed by a recent meta-analysis, but are applied to an "at risk" population, with possible implications in preventive and early diagnosis strategies. Leptin and IL-6, classically associated with obesity and inflammation, are here significantly associated with binge eating and have a trend to significance in the association with overall ED psychopathology. The work is methodologically well designed, concise and informative. I have the following comments that should be addressed in order to further enhance this already important piece of work.

Minor comments:

Abstract: Relevance for patients: I would be more hypothetical, adding "eventually" before improving line 9.

Intro pg 5 line 56. Instead of "or overvalued" more proper could be "and overvalued idea about weight...".

Intro pg 5 line 58. Something should be added, here about the trend to earlier onset of ED, rather than the increased incidence or prevalence which instead is more controversial.

Methods.

Questionnaires choice. Authors should explain why they did not use some other structured scale for ED symptoms, such as EDI-3 for example. EAT-26 is more a screening tool than a psychopathology evaluating one; so a reason could be the work aims at evaluating biomarkers use in a screening context. If this is the case, then it should be clearly stated.

EAT-26 score. Authors perform the analyses using total EAT-26 score. On top of it, it would be nice to see what comes out when using EAT-26 subscores, such as dieting or oral control.

Biomarkers. Another useful inflammation mediator that showed to be associated with ED symptoms in the same meta-analysis cited in the discussion from Solmi et al, is TNF-alpha.

Authors should explain why they did not include it in their work (budget limits? any

physiopathologic reason? or?).

Results.

Authors should also bring attention to the trend to significance of the EAT ($p=0.07$) association with IL-6. Due to the fact that the final sample size did not match the designed one, since several students refused blood sample or dropped for other reasons, it is possible this result is not significant due to small sample size.

Discussion.

Please double-check if no previous study at all investigated ED symptoms and biomarkers in non-clinical population.

Please add to the limitations: final sample size substantially different from the designed one - cross-sectional design - no complete inflammatory mediators panel.

2nd editorial decision

Ref.: Ms. No. JCTRes-D-16-00020R1

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Dear Mrs. Lofrano-Prado,

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was **FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.**

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at

<http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation."

Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Oct 02, 2016.

To submit a revision, go to <http://jctres.edmgr.com/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Rowan van Golen

Associate Editor

Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: Overall the manuscript improved from the first version, but some issues persist:

1. In the abstract and introduction the authors still address the markers for early diagnosis, from the nature of the study it cannot be determine if this markers spike early in the disease of eating disorders.
2. Although the authors control for BMI this issue was not completely address: Obese subjects have also been found to have increase reactants, please further discussed if BMI was taking into consideration for the inclusion or exclusion of this study.
3. The review did not clarify this issue completely: Please clarify if subjects with previous diagnoses or in treatment for ED where identified since this subjects could have screening tests negative but positive biomarkers or viceversa.

Reviewer #2: Authors addressed almost all main concerns and improved the manuscript, which

is now suitable for publication in my opinion.

Dear Professor Rowan:

We are grateful to you and to the reviewers for the time and effort dedicated to review our revised manuscript and offering additional comments. We have revised the manuscript according to these additional suggestions of the reviewers. Enclosed for your consideration is the revised version of the manuscript, entitled 'Non-traditional biomarkers of eating disorders symptoms among female college students' (JCTRes-D-16-00020).

We have addressed all additional issues raised by the two reviewers and a point-by-point explanation is also included. The comments of the reviewers are shown as 'Comment' and our answers and clarifications as 'Answer'. The changes are highlighted in the revised version of the manuscript. We believe that all of the additional issues and suggestions raised have been adequately addressed and the manuscript has been considerably enhanced.

Please do not hesitate to contact me if any additional information is needed.

Mara Cristina Lofrano do Prado, PhD

(On behalf of all other coauthors)

Reviewers' comments:

Reviewer #1

Comment: In the abstract and introduction the authors still address the markers for early diagnosis, from the nature of the study it cannot be determine if this markers spike early in the disease of eating disorders.

Answer: We agree with your comment and apologize for this mistake. As suggested the abstract and introduction were rewritten in order to adequately address this issue, as follow:

“...To beyond the classical eating disorders' symptoms (ED) related to unhealthy eating habits, which are not always recognized until late stage, ED may be also associated with non-traditional and objective biomarkers which may be an important screening tool supporting health professionals involved in ED prevention and treatment...” and

“...the identification of non-traditional and objective biomarkers associated with symptoms of ED may be, in a future, considered as an additional and new target for ED prevention and treatment...”

Comment: Although the authors control for BMI this issue was not completely address: Obese subjects have also been found to have increase reactants, please further discussed if BMI was taking into consideration for the inclusion or exclusion of this study.

Answer: We understand and agree with your comment. We know that obese individuals (independent of presenting symptoms of ED or not) are supposed to present higher circulating levels of the measured biomarkers, however we strongly believe that controlling the analyses by BMI, as suggested by you in the first round, support our conclusions, once even when controlled for BMI some associations remain. BMI was not considered for inclusion or exclusion criteria, but, in our opinion, the possible effect of the BMI on the outcomes has been adequately considered in this new version. We are open to discuss this issue if you judge that it is essential to accept our work for publication.

Comment: The review did not clarify this issue completely: Please clarify if subjects with previous diagnoses or in treatment for ED where identified since this subjects could have screening tests negative but positive biomarkers or viceversa.

Answer: Dear review, previous diagnosis or treatment for ED are exclusion criteria, however none of the volunteer's self-report diagnosis or treatment for ED. This information has been added in this new version, as follow: "...taking anti-inflammatory drugs, pregnancy, self-reported chronic disease, flu, allergy, illness the day of blood sampling and/or diagnoses or in treatment for ED (self-reported)..."

3rd editorial decision

Date: 9-Oct-2016

Ref.: Ms. No. JCTRes-D-16-00020R2

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Journal of Clinical and Translational Research

Dear Mrs. Lofrano-Prado,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research. The proofs of your manuscript will be sent to you as soon as possible. Please know that the manuscript will be proofread by the Editorial Board before publication to eliminate any typographic errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Rowan van Golen

Associate Editor

Journal of Clinical and Translational Research

Comments from the editors and reviewers:
