OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

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An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

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You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "The Associations Between Serum Concentrations of Irisin and Glucose-dependent Insulinotropic Polypeptide with Body Mass Index Among Women with and Without Polycystic Ovary Syndrome"

Author(s): Samira Behboudi-Gandevani, Mehdi Hedayati, Mohammad Ali Mansournia, Maryam Nazemipour, Maryam Rahmati, Fahimeh Ramezani Tehrani

Review Timeline:

Submit Date:	14 Dec 2020
Revised Date:	26 Apr 2021
Accepted Date:	28 Apr 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 1 Feb 2021

Dear AE,
In the manuscript entitled: “The association between serum concentration of irisin, glucose dependent insulin tropic polypeptide and BMI among women with and without polycystic ovary syndrome”, the authors investigated the association between BMI and serum concentration of irisin/glucose-dependent 6 insulin tropic polypeptide (GIP) in women with and without PCOS in the linear and nonlinear model. It is a well-written research work with an interesting subject. However, this study has some concerns which should be addressed before publication. Following are my comments:
Title
• please avoid using abbreviations in the title of a paper.
Abstract
• Please add the short background at the beginning of the abstract.
• In the keywords, add “Body mass index”
• The abstract should be 250 to 350 words.

• please select KEYWORDS (3-10) form MESH .
(http://www.nlm.nih.gov/mesh/MBrowser.html). “Glucose-dependent insulin tropic polypeptide” and “Irisin” are not in the meSH, please delete them or replace them with other words.
Introduction
• Please use the full name of DM and then abbreviation when it firstly appears in the text.
Method
• Please indicate when this study was conducted?
• How do you ensure that your sample size is sufficient for this study? Please provide sample size justification.
• Please explain how to sample for biochemical measurements.
• Please provide evidence for selecting exclusion criteria in this study.
Results:
• Please use the full name of WC and WHR and then abbreviation when it firstly appears in the text.
• Table 2: All abbreviated terms used in the tables should be defined in the footnote.
Thanks.

REFEREE: Reviewer | **Revision** (0) 26 Feb 2021

Dear AE,
I read the manuscript” The association between serum concentration of irisin, glucose dependent insulinotropic polypeptide and BMI among women with and without polycystic ovary syndrome”
- This is a well-written cross-sectional manuscript. The design of the study was good, including and excluding criteria, data collection, sources, and methods of selection of participants in both case and control groups were clarified
- Please define participants were from which region of Iran, were there representative of the whole Iranian population?
- In discussion, in the sentence “However, many factors have been associated with GIP responses, including age and gender (38), BMI, (17, 40) inflammatory cytokines, (41) insulin resistance and metformin treatment 17 which may have important effect on the findings”, please delete 17 after metformin treatment.
Thanks, sincerely

REFEREE: Reviewer | **Revision** (0) 28 Feb 2021

Dear AE,
The manuscript entitled as ” The association between serum concentration of irisin, glucose dependent insulinotropic polypeptide and BMI among women with and without polycystic ovary syndrome” is a well written manuscript about the association between irisin and GIP with body mass index in PCOS and non-PCOS women, issues that were assessed in a cross sectional-designed study . However, there are some minor point that needs to be corrected or completed.
Abstract:
1) Please add a brief introduction about the specific topic of interest of this study in the

background section of the abstract.

2) Please use uniform abbreviations for each item throughout the manuscript and Tables, i.e, “T2DM” or “DM” for diabetes mellitus, “L” or “l” for liter, ….

Method and methods:

1) It is suggested to prepare more separate sections with appropriate subtitles in the material and method part i.e. study population, definitions, ….. . In this line it is better to add a separate section named as “Definitions” and state all definitions such as Oligo/anovulation, clinical hyperandrogenism , and biochemical hyperandrogenism in that section.

2) Details of anthropometric measurements should be mentioned in the material and method section.

3) The complete characteristics including countries of the manufacturers of all the assay kits and instruments should be provided, similar to (ZellBio GmbH, Germany) that is mentioned for irisin and GIP.

4) Please add a statement regarding the monitoring of accuracy of assays.

5) For intra- and inter-assay CVs of TT assay, 3 number are presented (3.6% and 6.0%, and 3.2%). What is the third number related to?

6) What is the inter-assay CVs for irisin and GIP?

7) It is suggested to replace “immunoenzymometric” by “enzyme immunometric assay” which is more used in scientific articles.

8) The sensitivity of the assay kit and results of GIP should be provided in the same measurement unit, i.e. ng/mL or Pg/mL both in the text and Table.

Results:

1) Please add units to axis of plots in figurers 1 and 2.

2) Change the abbreviation of interquartile range from IQ to IQR in the footnote of Table 1 and define it.

3) Complete statement of SHBG should be written in the footnote of Table 1.

4) Table 2 is a small table with limited data that can be presented in the text, so it is recommended that not to present this data in tabular format.

5) Delete the term “basic” in the first line of result section.

Discussion:

1) It is suggested to replace “pathology” by “pathogenesis” in the 6th line of discussion.

2) Please present the complete form of GLUT4.

3) In the discussion the authors mentioned that one of the reasons for discrepant results of different studies may be related to gender difference, while it seems that all studies that were referred to in the previous paragraph to this statement were conducted among women.

4) The format of reference citation should be uniform in the manuscript so it is better to delete year of publication (2011) from this sentence of the manuscript “Pontikis et al. (2011) investigated the secretion of GIP between age matched obese and lean patients with PCOS after oral glucose tolerance tests (OGTT).” In the discussion section.

5) The conclusion of the study can be written in a better foe example this sentence “Taken together, we hypothesized that the positive correlation of circulating irisin with obesity may be nullified by other factors in the pathological states of obesity.” hat is written in the 4th paragraph of the manuscript can be revised and used to strength the conclusion.

General:

1) The manuscript has many punctuation errors. For example see the following sentence:

“However, many factors have been associated with GIP 134responses, including age and gender (38), BMI, (17, 40) inflammatory cytokines, (41)insulin resistance and metformin treatment 17 which may have an important effect on the findings. Well-designed with appropriate sample size are warranted to explore these associations.”
Comma after (38), comma before (17, 40), absence of space between (41) and insulin, not justified number 17 in this sentence, … . Hence please check throughout the manuscript and correct punctuation errors.
2) The manuscript needs better English language editing.
Thanks.

REFEREE: Associate Editor | **Revision (0)** 28 Feb 2021

Dear EIC,
If the authors provide careful revisions and point by point responses, the manuscript will be acceptable for publication.
Thanks.

REFEREE: EIC | **Revision (0)** 1 Mar 2021

Dear Authors,
Based on the reviewers' comments the manuscript needs Minor Revision.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Response (R) to reviewer comments (C)

Many thanks for the evaluation the paper and sending us your valuable and precise comments and also the opportunity to revise and resubmit the manuscript. We have carefully considered all comments and hereby submit a revised version; all changes red highlighted in the text. We hope our revisions meet your expectations. Looking forward to hearing from you at your earliest convenience,

Sincerely yours,

Corresponding author
Professor of Obstetrics, Gynecology and Reproductive Endocrinology
Director, Reproductive Endocrinology Research Center,
Research Institute for Endocrine Sciences,
Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Reviewers' Comments:

Reviewer 1:

In the manuscript entitled: “The association between serum concentration of irisin, glucose dependent insulin tropic polypeptide and BMI among women with and without polycystic ovary syndrome”, the authors investigated the association between BMI and serum concentration of irisin/glucose-dependent 6 insulin tropic polypeptide (GIP) in women with and without PCOS in the linear and nonlinear model. It is a well-written research work with an interesting subject. However, this study has some concerns which should be addressed before publication. Following are my comments:
Title
• please avoid using abbreviations in the title of a paper.

R: It was revised as you wished.

Abstract
• Please add the short background at the beginning of the abstract.

R: It was added as you wished.

• In the keywords, add “Body mass index”

R: It was added as you wished.

• The abstract should be 250 to 350 words.

R: It was revised accordingly.

• please select KEYWORDS (3-10) form MESH .

(http://www.nlm.nih.gov/mesh/MBrowser.html). “Glucose-dependent insulin tropic polypeptide” and “Irisin” are not in the meSH, please delete them or replace them with other words.

R: It was revised accordingly.

Introduction
• Please use the full name of DM and then abbreviation when it firstly appears in the text.

R: It was revised accordingly.

Method
• Please indicate when this study was conducted?

R: It was added as you wished.

• How do you ensure that your sample size is sufficient for this study? Please provide sample size justification.

R: We calculated the power of the test for the study sample size by assuming irisin variable as a primary outcome. Group sample sizes of 159 and 82 achieved 82.9% power to reject the null hypothesis of equal means when the population mean difference is 25.0 with a standard deviation for both groups of 65.0 and with a significance level (alpha) of 0.050 using a two-sided two-sample equal-variance t-test. It was highlighted in the text.

• Please explain how to sample for biochemical measurements.

R: It was added as you wished.

• Please provide evidence for selecting exclusion criteria in this study.

R: It was added as you wished.

Results:
• Please use the full name of WC and WHR and then abbreviation when it firstly appears in the text.

R: It was revised accordingly.

• Table 2: All abbreviated terms used in the tables should be defined in the footnote.

R: Based on the reviewer comment, the results of table 2 replaced to the main text.

Reviewer 2:
Dear associated editor
I read the manuscript" The association between serum concentration of irisin, glucose dependent insulinotropic polypeptide and BMI among women with and without polycystic ovary syndrome"
This is a well written cross-sectional manuscript. The design of the study was good, including and excluding criteria, data collection, sources and methods of selection of participants in both case and control group were clarified

C: Please define participants were from which region of Iran, were there representative of whole Iranian population?

R: Thank you for valuable comment. Since, this study was performed among women aged who were known cases of PCOS, referred from outpatient endocrinology clinic in Tehran from March 2015- March 2018, therefore they are not representative of Iranian population. This point was added to the limitation of study.

In discussion, in the sentence "However, many factors have been associated with GIP responses, including age and gender (38), BMI, (17, 40) inflammatory cytokines, (41) insulin resistance and metformin treatment 17 which may have important effect on the findings", please delete 17 after metformin treatment.

R: It was revised accordingly.

Reviewer 3:

The manuscript entitled as " The association between serum concentration of irisin, glucose dependent insulinotropic polypeptide and BMI among women with and without polycystic ovary syndrome" is a well written manuscript about the association between irisin and GIP with body mass index in PCOS and non-PCOS women, issues that were assessed in a cross sectional-designed study . However, there are some minor point that needs to be corrected or completed.
Abstract:
1) Please add a brief introduction about the specific topic of interest of this study in the background section of the abstract.

R: It was added as you wished.

2) Please use uniform abbreviations for each item throughout the manuscript and Tables, i.e, "T2DM" or "DM" for diabetes mellitus, "L" or "l" for liter, … .

R: It was revised accordingly.

Method and methods:
1) It is suggested to prepare more separate sections with appropriate subtitles in the material and method part i.e. study population, definitions, ….. . In this line it is better to add a separate section named as “Definitions” and state all definitions such as Oligo/anovulation, clinical hyperandrogenism , and biochemical hyperandrogenism in that section.

R: Thank you for the valuable comment. It was revised accordingly.

2) Details of anthropometric measurements should be mentioned in the material and method section.

R: It was added as you wished.

3) The complete characteristics including countries of the manufacturers of all the assay kits and instruments should be provided, similar to (ZellBio GmbH, Germany) that is mentioned for irisin and GIP.

R: It was added as you wished.

4) Please add a statement regarding the monitoring of accuracy of assays.

R: It was added as you wished.

5) For intra- and inter-assay CVs of TT assay, 3 number are presented (3.6% and 6.0%, and 3.2%). What is the third number related to?

R: The intra-assay and inter-assay coefficients of variation for TT were 3.6% and 6.0%. It was corrected accordingly.

6) What is the inter-assay CVs for irisin and GIP?

R: It was added as you wished.

7) It is suggested to replace “immunoenzymometric” by “enzyme immunometric assay” which is more used in scientific articles.

R: It was revised accordingly.

8) The sensitivity of assay kit and results of GIP should be provided in same measurement unit, i.e. ng/mL or Pg/mL both in the text and Table.

R: It was revised accordingly.

Results:
1) Please add units to axis of plots in figurers 1 and 2.

R: It was added as you wished.

2) Change the abbreviation of interquartile range from IQ to IQR in the footnote of Table 1 and define it.

R: It was revised accordingly.

3) Complete statement of SHBG should be written in the footnote of Table 1.

R: It was revised accordingly.

4) Table 2 is a small table with limited data that can be presented in the text, so it is recommended that not to present this data in tabular format.

R: It was revised accordingly.

5) Delete the term “basic” in the first line of result section.

R: It was revised accordingly.

Discussion:

1) It is suggested to replace “pathology” by “pathogenesis” in the 6th line of discussion.

R: It was replaced accordingly.

2) Please present the complete form of GLUT4.

R: It was revised accordingly.

3) In the discussion the authors mentioned that one of the reason for discrepant results of different studies may be related to gender difference, while it seems that all studies that were referred to in the previous paragraph to this statement were conducted among women.

R: thank you for the comment. It was corrected.

4) The format of reference citation should be uniform in the manuscript so it is better to delete year of publication (2011) from this sentence of the manuscript “Pontikis et al. (2011) investigated the secretion of GIP between age matched obese and lean patients with PCOS after oral glucose tolerance tests (OGTT).” In the discussion section.

R: It was revised accordingly.

5) The conclusion of the study can be written in a better for example this sentence “Taken together, Taken together, based on the findings of these studies, it is hypothesized that the positive correlation of circulating irisin with obesity may be nullified by other factors in the pathological states of obesity.” that is written in the 4th paragraph of the manuscript can be revised and used to strength the conclusion.

R: It was revised accordingly.

General:
1) The manuscript has many punctuation errors. For example see the following sentence: “However, many factors have been associated with GIP 134responses, including age and gender (38), BMI, (17, 40) inflammatory cytokines, (41)insulin resistance and metformin treatment 17 which may have important effect on the findings. Well-designed with appropriate sample size are warranted to explore these associations.”
Comma after (38), comma before (17, 40), absence of space between (41) and insulin, not justified number 17 in this sentence, … . Hence please check throughout the manuscript and correct punctuation errors.

R: Agree, It was revised accordingly.

2) The manuscript needs better English language editing.

R: Thank you for the comment, It has been edited once more.

Associate Editor's Comments:

Associate Editor 1:
If the authors provide careful revisions and point by point responses, the manuscript will be acceptable for publication.

EIC Decision:

Based on the reviewers' comments the manuscript needs Minor Revision.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision (1)** 15 Mar 2021

Dear AE,
Thank you for the corrections performed on revision (0) of the manuscript, however, there are still minor points that need to be corrected.
Abstract:
1) As linguistic editing, it is suggested to change the first sentence of the abstract is below: “Adipocytokines may act as connecting factors between obesity and polycystic ovary syndrome (PCOS). It has been suggested that irisin, a recently described cytokine secreted from skeletal muscles and glucose-dependent insulinotropic polypeptide (GIP), an incretin hormone that induces cytokine expression may play key roles in favoring obesity in these women”
1) In the 5th line of the abstract delete the complete term of PCOS, since it was presented earlier.
2) “IR” that was used in the conclusion section of the abstract should be written in complete form because it was not presented earlier.
3) In key words, please write “Insulin Resistance” as “Insulin resistance”.
Background:
1) In this sentence: “The syndrome is highly associated with by reproductive and metabolic disturbance”, please delete the preposition “by”.
2) It is suggested to change “antidiabetic” to “anti-diabetic”.
3) It is suggested to change this sentence as below:
4) “The women’s weight and height were measured using a standard apparatus and wearing light clothes without shoes to the nearest 0.1 kg and 0.5 cm respectively.”
“The weight and height with light clothing without shoes were measured by standard devices to the nearest 0.1 kg and 0.5 cm, respectively.”
Material and methods
1) The calculation of WHR is written twice in the first paragraph of “ Clinical and laboratory measurements”
2) In the second paragraph of the “Clinical and laboratory measurements”, please put space between “hormone” and “binding”; it was written as Sex hormone-binding globulin”.
3) In the second paragraph of the “Clinical and laboratory measurements”, the space after “6%” should be deleted.
4) The term "ELISA" should be written in complete form for the first time of use.
5) It is suggested to introduce the abbreviation “CV” after the first-time use of “coefficient of variation” because it is used in the next sentences, too.

6) Please add “and” after “irisin” in the last sentence of the Clinical and Biochemical measurements section.
7) It is suggested using “Term” in plural form in the subtitle of “Term definition”.
8) Thank you for mentioning the details of sample size calculation, but it is suggested that the sentence written about the sample size calculation in the first paragraph of the statistical analysis be written as short as possible.
Discussion
1) In the 5th paragraph of the discussion, delete one of the spaces between “GIP” and “between”.
2) In the 5th paragraph of the discussion, it is suggested to use “IR” instead of “insulin resistance” because “IR” was previously introduced and used.
3) In the 6th paragraph of the discussion, it seems that “the tertiary center of Tehran” is not a proper term, and “a tertiary clinic in Tehran” is suggested.
4) Please add the possible strengths of this study to the manuscript.
5) The conclusion of the manuscript is broad and suggests the need for future studies, messages that have not been derived directly from this study. The conclusion should be revised. I think that the conclusion is written in revision (0) was better compared to the current one and needs minor revision.
Thanks.

REFEREE: Reviewer | **Revision (1)** 15 Mar 2021

Dear AE,
Thanks for responding to the questions and addressing all comments.
Regards.

REFEREE: Associate Editor | **Revision (1)** 3 Apr 2021

Dear EIC,
According to the reviewers' comments, the revised manuscript needs to have point-by-point minor revisions.
Furthermore, the main need of this manuscript is English language editing.
It would be appreciated if, in the file of response to reviewers, the exact address (pages and lines) of any correction or changes that have been made in the manuscript would be written; this issue provides better and faster peer review.
Thanks.

REFEREE: EIC | **Revision (1)** 3 Apr 2021

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Response (R) to reviewer comments (C)

Many thanks for the evaluation the paper and sending us your valuable and precise comments and also the opportunity to revise and resubmit the manuscript. We have carefully considered all comments and hereby submit a revised version; all changes red highlighted in the text. We hope our revisions meet your expectations. Looking forward to hearing from you at your earliest convenience,

Sincerely yours,

Reviewers' Comments:

Reviewer 2:

Thank you for corrections performed on revision of the manuscript, however, there are still minor points that need to be corrected.

Abstract:

1) As linguistic editing , it is suggested to change the first sentence of the abstract as below:

“Adipocytokines may act as connecting factors between obesity and polycystic ovary syndrome (PCOS). It has been suggested that irisin, a recently described cytokine secreted from skeletal muscles and glucose-dependent insulinotropic polypeptide (GIP), an incretin hormone that induces cytokine expression may play key roles in favoring obesity in these women”

R: It was replaced as you wished.

1) In the 5th line of the abstract delete the complete term of PCOS, since it was presented earlier.

R: It was corrected.

2) “IR” that was used in the conclusion section of the abstract should be written in complete form because it was not presented earlier.

R: It was corrected.

3) In key words, please write “Insulin Resistance” as “Insulin resistance”.

R: It was corrected.

Background:

1) In this sentence: “The syndrome is highly associated with by reproductive and metabolic disturbance”, please delete preposition “by”.

R: It was corrected.

2) It is suggested to change “antidiabetic” to “anti-diabetic”.

R: It was corrected.

3) It is suggested to change this sentence as below:

“The women’s weight and height were measured using a standard apparatus and wearing light clothes without shoes to the nearest 0.1 kg and 0.5 cm respectively.”

“The weight and height with light clothing without shoes were measured by standard devices to the nearest 0.1 kg and 0.5 cm, respectively.”

R: It was corrected.

Material and methods

1) The calculation of WHR is written twice in the first paragraph of “ Clinical and laboratory measurements”

R: It was corrected.

2) In the second paragraph of the “Clinical and laboratory measurements”, please put space between “hormone” and “binding”; it was written as Sex hormonebinding globulin”.

R: It was corrected.

3) In the second paragraph of the “Clinical and laboratory measurements”, the space after “6%” should be deleted.

R: It was corrected.

4) The term "ELISA" should be written in complete form in for the first time of use.

R: It was corrected.

5) It is suggested to introduce abbreviation “CV” after first time use of “coefficient of variation” because it is used in the next sentences, too.

R: It was corrected.

6) Please add “and” after “irisin” in the last sentence of the Clinical and Biochemical measurements section.

R: It was corrected.

7) It is suggested using “Term” in plural form in the subtitle of “Term definition”.

R: It was corrected.

8) Thank you for mentioning the details of sample size calculation, but it is suggested that the sentence written about the sample size calculation in the first paragraph of the statistical analysis be written as short as possible.

R: It was revised as you wished.

Discussion

1) In the 5th paragraph of the discussion, delete one of the spaces between “GIP” and “between”.

R: It was corrected.

2) In the 5th paragraph of the discussion, it is suggested to use “IR” instead of “insulin resistance” because “IR” was previously introduced and used.

R: It was corrected.

3) In the 6th paragraph of the discussion, it seems that “the tertiary center of Tehran” is not a proper term, and “a tertiary clinic in Tehran” it is suggested.

R: It was corrected.

4) Please add the possible strengths of this study to the manuscript.

R: It was added to the discussion section.

5) The conclusion of the manuscript is broad and suggests need for future studies, messages that have not derived directly from this study. The conclusion should be revised. I think that the conclusion written in revision (0) was better compared to the current one and needs minor revision.

R: It was revised as you wished.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (2) 18 Apr 2021

Dear EIC,
Thanks for the corrections performed on revision (1) of the manuscript. I think that this manuscript can be accepted to publish in IJEM after correcting the following minor points:
- First: Authors tried to mention some strengths for their study in response to the reviewer,s comment and mentioned that: “The strength of this study is its accurate laboratory measurements markers and statistical analysis used both linear and nonlinear model, adjusted for the age that could help to reach more precise results.”
"Accurate laboratory measurement" is an inevitable necessity, not the power of the study. If the authors mean such emphasis on “precise laboratory markers”, this is not entirely in agreement. Therefore, it is suggested to revise the written paragraph about the strength of the study.
The Following sentence may be considered as a suggestion:
“Measurement of relatively new laboratory markers and analysis by both linear and nonlinear statistical models could be considered as the strengths of this study.
- Second: As mentioned in previous rounds of peer review, the manuscript has sub-optimal linguistic quality. In this line, it is suggested to replace the paragraph of conclusion by the following one:
“This study showed that Iris and GIP have no association with BMI in women with or without PCOS. This finding could help to better understand the underlying pathophysiological status of PCOS, insulin resistance, and obesity-related disorders. To confirm these findings, another large cohort study are needed.”
Thanks.

REFEREE: EIC | **Revision** (2) 18 Apr 2021

Dear Authors,
The manuscript will be accepted for publication in the IJEM after revision.
Thanks.

OPEN PEER REVIEW

Revision (3)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Response (R) to reviewer comments (C)

Many thanks for the evaluation the paper and sending us your valuable and precise comments and also the opportunity to revise and resubmit the manuscript. We have carefully considered all comments and hereby submit a revised version; all changes red highlighted in the text. We hope our revisions meet your expectations. Looking forward to hearing from you at your earliest convenience,

Sincerely yours,

Reviewers' Comments:

Reviewer 2:

Associate Editor 1:
Thank you for corrections performed on revision (1) of the manuscript. I think that this manuscript can be accepted to publish in IJEM after correcting these following minor points:

First: Authors tried to mention some strengths for their study in response to reviewer,s comment and mentioned that: “The strength of this study is its accurate laboratory measurements markers and statistical analysis used both linear and nonlinear model, adjusted for age that could help to reach more precise results.”
"Accurate laboratory measurement" is an inevitable necessity, not the power of study. If the authors mean such emphasis on “precise laboratory markers”, this is not entirely in agreement. Therefore, it is suggested to revise the written paragraph about the strength of the study.
Following sentence may be considered as a suggestion:
“Measurement of relatively new laboratory markers and analysis by both linear and nonlinear statistical models could be considered as the strengths of this study.

R: Agree, it was revised based on this comment.

Second: As mentioned in previous rounds of peer review, the manuscript have sub-optimal linguistic quality. In this line, it is suggested to replace the paragraph of conclusion by the following one:
“This study showed that Iris and GIP have no association with BMI in women with or without PCOS. This finding could help to better understand the underlying pathophysiological status of PCOS, insulin resistance, and obesity-related disorders. To confirm these findings, another large cohort studies are needed.”

R: It was revised based on this comment.

OPEN PEER REVIEW

Revision (3)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision** (3) 28 Apr 2021

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.