OPEN PEER REVIEW

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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.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
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- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

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

Journal of Comprehensive Pediatrics
Article DOI: 10.5812/compreped.107272
Published in: Journal of Comprehensive Pediatrics: 11(4); e107272

Peer Review Report for "Is It Necessary to Weight Loss in Obese Boys with Small Penile Length? A Case-Control Study"

Author(s): Sadra Rezakhaniha, Bijan Rezakhaniha, Nahid Aarabi, Soheila Siroosbakht

Review Timeline:

Submit Date: 7 Jul 2020
Revised Date: 31 Aug 2020
Accepted Date: 14 Oct 2020

Revision (0)

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

Arezoo Haseli: Reviewer | **Revision** (0) — 22 Jul 2020

Dear AE,
This is an interesting topic that is likely to be of interest to the readers of this journal. Some of the claims/points made in this article need to be better supported with other statistical tests such as Odd Ratio, sensitive analysis, and controlling of confounders.
However, there are also some major issues with the article in its current form. A thorough revision of methods and analytic tests may help to create a more coherent and valuable article. I have made minimal comments throughout...
Thanks.

REFEREE: Reviewer | **Revision** (0) — 23 Jul 2020

Dear AE,
I think this manuscript advances health care worldwide and improves experiences, but needs some improvement.
Abstract:
- In line 1 “today” is better change to “nowadays”.
- We are not allowed to use any abbreviation word without definition for the first time: BMI
Introduction:

- Introduction is long. The sentences in last paragraph can be summarized.
- There is no need for definitions that are not relevant to the purpose of the study (line 4 and 8).

Methods:

- Methods section is good. Inclusion and exclusion criteria should be state before selecting samples and number of subjects.

Results:

- Results section is clear and precise.

Discussion:

- Paragraph one; line 3-4 should be revised. So it is important to know the age related penis size and accurate measurements in distinguishing true micropenis children “distinguish with which group? Adds “With concealed penis”.
- Line 9 “develops” change to “development”.
- Paragraph 2; line 2, “subfertility” change to sub-fertility”.
- Paragraph 6 line 8 and 9; is better to be omitted.
- Paragraph 8; line 3,4,5 should be revised.
- Paragraph 10 should be summarized. Line 1 and 2 is repetitive.
- References and tables were designed as the journal rules.

Thanks.

REFEREE: Reviewer | **Revision** (0) 25 Jul 2020

Dear AE,

I thank you for all your efforts . This manuscript studies the micropenis in obese and non-obese children which is an important issue.

the manuscript needs some correction.

1. Title is properly selected.
2. In the abstract section BMI should be expanded for the first time (no abbreviation).
3. In introduction line 4 and 8 is not related to the manuscripts. It is better deleting those.
4. Methods part is good.
5. Results part is good.
6. In the discussion part you should write the main(s) finding(s) at first and then allude to other studies.

In paragraph 1, the development of micropenis instead of develops micropenis.

Paragraph 8,should be reviewed and corrected.

Also lines 1 and 2 in paragraph 10 must be deleted.

7. Tables are accurate and clear
8. References and citations are correct.

Thanks.

REFEREE: Associate Editor | **Revision** (0) 27 Jul 2020

Dear EIC

The reviewer(s) have recommended publication, but also suggest some major revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.

Kind regards,

REFEREE: EIC | **Revision** (0) 27 Jul 2020

Dear Author,

The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.

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.

According to precious opinion of reviewers; I state that:

According to the reviewer 1:
I thank you for all your efforts . This manuscript studies the micropenis in obese and non-obese children which is an important issue.
the manuscript need some correction.
Q1. Title is properly selected.

R1. Thanks
Q2. In abstract section BMI should be expanded in first time (no abbreviation).

R2. BMI was expanded in abstract section (body mass index).
Q3. In introduction line 4 and 8 is not related to the manuscripts. It is better deleting those.

R3. Line 4 and 8 were deleted.
Q4. Methods part is good.

R4. Thanks
Q5. Results part is good.

R5. Thanks
Q6. In the discussion part you should write the main(s) finding(s) at first and then allude to other studies.
In paragraph 1, development of micropenis instead of develops micropenis.
Paragraph 8 should be reviewed and corrected.
Also lines 1 and 2 in paragraph 10 must be deleted.

R6. In paragraph 1, “develops of micropenis” was changed to “development of micropenis”.

Paragraph 8 was reviewed and corrected.

Lines 1 and 2 in paragraph 10 were deleted.

Q7. Tables are accurate and clear.

R7. Thanks
Q8. References and citations are correct.

R8. Thanks

According to the reviewer 2:
I think this manuscript advances health care worldwide and improve experiences.
Abstract:
Q1. In line 1 “today” is better change to “nowadays”.

R1. In line 1 “today” was changed to “nowadays”.
Q2. We are not allowed to use any abbreviation word without definition for the first time: BMI

R2. Body mass index was mentioned in abstract section.
Introduction:
Q3.Introduction is long. The sentences in last paragraph can be summarized.

R3. Introduction was summarized as possible as.
Q4.There is no need for definitions that are not relevant to the purpose of the study (line 4 and 8).

R4. In paragraph 1, line 4 & 8 was deleted.
Methods:
Q5.Methods section is good. Inclusion and exclusion criteria should be state before selecting samples and number of subjects.

R5. Thank you. Inclusion and exclusion criteria were stated before selecting samples and number of subjects.

Results:
Q6. Results section is clear and precise.

R6. Thank you
Discussion:
Q7. Paragraph one; line 3-4 should be revised. So it is important to know the age related penis size and accurate measurements in distinguishing true micropenis children “distinguish with which group? Adds “With concealed penis”.

R7. Paragraph one; lines 3-4 were revised and “With concealed penis”was added.
Q8. Line 9 “develops” change to “development”.

R8. Line 9 “develops” was changed to “development”.
Q9. Paragraph 2; line 2 “subfertility” change to sub-fertility”.

R9. Paragraph 2; line 2, “subfertility” was changed to sub-fertility”.
Q10. Paragraph 6 lines 8 and 9; is better to be omitted.

R10. Paragraph 6 lines 8 and 9; were omitted.
Q11. Paragraph 8; line 3,4,5 should be revised.

R11. Paragraph 8; line 3,4,5 were revised.
Q12. Paragraph 10 should be summarized. Line 1 and 2 is repetitive.

R12. Paragraph 10 was summarized. Line 1 and 2 was deleted.
Q13. References and tables were designed as the journal rules.

R13. Thank you.

According to the reviewer 3:
Q1. This is an interesting topic that is likely to be of interest to the readers of this journal. Some of the claims/points made in this article need to be better supported with other statistical tests such as Odd Ratio, sensitive analysis, and controlling of confounders.
However, there are also some major issues with the article in its current form. Thorough revision of methods and analytic tests may help to create a more coherent and valuable article. I have made minimal comments throughout....

R1. Thank you for your informative tips. The lack of sensitive analysis was mentioned as one of the limitation of study in discussion section. However, the manuscript revised totally, especially in methods and results section and also, English editing was done. The results in this article such as the correlation of height and testosterone to penile length in obese and non-obese groups that were statistically significant with Pearson's correlation coefficient (r) test were supported and analyzed with a logistic regression model to evaluate the odds ratio (OR) with confidence intervals 95% (CI 95%).

Best regards

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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) — 5 Aug 2020

Dear AE,
All the points mentioned have been changed by the author.
Thank you

REFEREE: Reviewer | **Revision** (1) — 8 Aug 2020

Dear AE,
The author's responses to my comments were precise and correct.
Thank you.

REFEREE: Reviewer | **Revision** (1) — 14 Aug 2020

Dear AE,
The author has not corrected most of the comments in the text including:
- Clearly define all potential confounders and effect modifiers. Give diagnostic criteria, if applicable.
- How did you calculate the sample size? Explain it.
- Describe statistical methods, used to control for confounding.
- Control of confounders is an important point in case-control studies.
- Describe any sensitivity analyses.
- Please add a flow diagram.
- Did you have missing data?
- Please explain confounder and test to confounder-adjusted.
- Before limitation, express the strengths of this study.

Please, the author/s answer all comments in the text.
Thanks.

REFEREE: Associate Editor | **Revision** (1) — 15 Aug 2020

Dear EIC,
Thanks for revising the manuscript. The authors revised the manuscript based on the comments of 2 reviewers but one of reviewers distinguished that manuscript still needs revision.
Thanks.

REFEREE: EIC | **Revision (1)** 15 Aug 2020

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.

Reviewers' Comments:

Reviewer 1:
The author has not corrected most of the comments in the text including:
Q. Clearly define all potential confounders and effect modifiers. Give diagnostic criteria, if applicable.
How did you calculate the sample size? Explain it.
Describe statistical methods, used to control for confounding.
control of confounders is an important point in case-control studies.
Describe any sensitivity analyses.
Please add a flow diagram.
Did you have missing data?
please explain confounder and test to confounder-adjusted.
Before limitation, express the strengths of this study.
Please, the author/s answer all comments in the text.

R. thank you for informative tips

Methods and results section were revised totally.

On the base of the previous studies, we found the most variables of micropenis and we offer recommendations to address these confounders: abnormality of penis such as curvature, history of taking corticosteroids, chronic disease and endocrine disease such as thyroid disease and growth hormone deficiency, undescending testis, and atrophy of testis, varicocele and any form of hypospadiasis. Non-essential and acquired factors were excluded by considering the inclusion and exclusion criteria. We focused on a selection of main and potential confounders in isolated micropenis in healthy prepubertal children: age, sex steroid factors, height, weight, BMI.

Minimize and control of confounders was performed in three ways: 1- restriction the study population, 2- matching the two comparison groups and 3- stratifications of pooled data.

Minimize and control of confounding in study design was done by restriction the study population to male prepubertal children 8-13 years. Age distributions were similar in the compared groups, so that cofounding would be minimized. Furthermore, we tried the study groups did not differ with respect to possible confounders such as age, sex steroid factors, height, weight, BMI by matching the two comparison groups. The Cochran-Mantel-Haenszel method was used for confounders control and statistical analysis was performed by multiple variable regression analysis.
For effect modification, pooled data converted to stratum-specific measures and stratified analysis was performed. Table 4 was added.
To evaluate the results, sensitivity analysis was performed that measures how the impact of uncertainties of input variables can lead to uncertainties on the output variables. In this study due to variety of parameters, the one-at-a-time (OAT) technique has been used to reconsider the correlation of height, Testosterone, weight and estradiol on the penile length. The sensitivity analysis-graph for each variable has analyzed in the given charts.

By reviewing the previous studies, by using formula, $n=\frac{\left[Z_{1-\alpha/2}+\sqrt{\left(1-\frac{1}{C}\right)\acute{P}\left(1-\acute{P}\right)}+Z_{1-\beta}\sqrt{P_1\left(1-P_1\right)+\frac{P_\circ\left(1-P_\circ\right)}{C}}\right]^2}{\left(P_1-P_\circ\right)^2}$, $P_\circ$= 30%, OR=2, $\alpha=5\%$ and $ß=10\%$, C=1.5. Therefore, at least 56 non-obese children and 84 obese children were considered for study.

Flowchart of study was added at the end manuscript.

Most studies have focused on penis size to get the normal size of society in young men and especially term or preterm neonates, but present study was conducted to assess pre-pubertal children with micropenis. To date, few studies have focused on true micropenis and its relationship to weight and hormonal levels. This study investigated the relation between anthropometric measures, testosterone and estradiol in pre-pubertal children with micropenis to get clear suggestions for this issue, which worries both physicians and parents.

All comments were added in the text.

Reviewer 2:

Q1. All the points mentioned have been changed by the author.

R1. Thank you for your attention.

Reviewer 3:

Q1.The author's responses to my comments were precise and correct.

R1. Thank you for your attention.

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.

Arezoo Haseli: Reviewer | **Revision** (2) 12 Oct 2020

Dear AE,
All the points mentioned have been changed by the author.
Thanks.

REFEREE: Associate Editor | **Revision** (2) 14 Oct 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (2) 14 Oct 2020

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