

Iodine nutrition level and thyroid function in pregnant women in the Yongchuan district of Chongqing

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Handling editor:

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Ref.: Ms. No. JCTRes-D-22-00028

Analysis of iodine nutrition level and thyroid function of pregnant women in

Yongchuan, Chongqing

Journal of Clinical and Translational Research

Dear Xiao Zhenghua Xiao,

Reviewers have now commented on your paper; two reviewers have recommended a reject and two reviewers have recommended a major revision. 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 and attached to this decision letter.

The editorial board specifically wishes you to address the comment of reviewer 3 and the first comment of reviewer 4 pertaining to spot urinalysis in individuals for the determination of iodine deficiency. We have a serious issue with propagating information that is contrary to clearly established guidelines that in turn are backed by extensive research. Please make sure that this issue is adequately addressed in the revision.

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 submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by May 31, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> 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

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #2: Please see my comments below:

1) Abstract: this is not properly written. The methods were not described explicitly. English needs to be improved.

2) Introduction: what is the research gap? The current maternal iodine status in China is not discussed. The authors are recommended to include the following references as part of their reference list:

Ma, Z.F. and Skeaff, S.A., 2017. Assessment of population iodine status. In Iodine deficiency disorders and their elimination (pp. 15-28). Springer, Cham.

Yu, Zengli, et al. "Mild-to-moderate iodine deficiency in a sample of pregnant women and salt iodine concentration from Zhejiang province, China." *Environmental Geochemistry and Health* 42.11 (2020): 3811-3818.

3) Methods: the inclusion, exclusion criteria and study protocol were not clearly expressed and logically connected. The authors are recommended to include the following references in their methods as part of their reference list:

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4) Results: Please start with the main findings, followed by the secondary findings.

5) The results were poorly written, and did not address the research questions sufficiently.

6) Discussion: Poorly structured, lack of references to the previous study. Please compare the findings in the study with other published studies. The authors are recommended to include the following references as part of their reference list:

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7) Please improve the English throughout the manuscript.

Reviewer #3: I see a number of concerns with how the authors present the results, and their suggestion to incorporate urinary iodine testing into routine obstetrics. Urinary iodine concentration is not a good measure of iodine status at the individual level and is recommended for evaluation populations at a group level.

Reviewer #4: Summary: This is a cross-sectional study of 300 pregnant women from Chongqing, China, assessing urinary iodine levels and thyroid function tests measured in 100 women in each trimester. Strength of the study includes measurement of iodine and thyroid function concurrently in different trimesters. Limitations include cross-sectional study design with single point of laboratory measurements and lack of thyroid antibody assessment. Overall, the findings of this study confirms results of other previous studies regarding association between iodine status and thyroid function in pregnant women. However, the conclusion may be somewhat inappropriate given current limitations in individual-level iodine assessment. Discussion also needs to be expanded.

Specific comments:

1. The conclusion (both in abstract and in discussion) where the authors recommend routine monitoring of urinary iodine levels in pregnant women is currently inappropriate, as there is no good individual level markers of long-term iodine status at this time. As the authors mention in the manuscript, urinary iodine levels are good markers of recent iodine intake and it varies significantly from day to day and depending on food intake. WHO currently recommends median UIC as a marker of population-level iodine status. Therefore, checking spot UIC in pregnant women once may not be adequate to diagnose iodine deficiency or excess.

2. Was there any Ethics board approval for the study? Please include information regarding Ethics board approval in the manuscript.

3. The descriptive results of the demographics of women in each trimester (including table 1) in Materials and Methods section would be more appropriate in Results section.

4. Was the thyroid function intervals reported specific for pregnant women? As the authors discuss in discussion, TSH tends to be lower in early pregnancy due to various factors. The

reference ranges provided in the materials and methods section appear to be similar to those for non-pregnant adults. Were the reference ranges provided developed specifically for pregnant women or were the same reference ranges for non-pregnant adults used for diagnosis of thyroid dysfunction?

5. What is the environmental iodine level in Chongqing area? My understanding is that water iodine content differs from area to area in China and the difference can be quite significant. This may affect the findings regarding urinary iodine levels in this study, as well as comparison study done in Zhejiang mentioned in discussion (third paragraph).

6. "FSH" should be corrected to "TSH" in the first line of the 4th paragraph in discussion (line 8).

7. The authors report "It may be due to the direct effect of iodine on the pituitary and hypothalamus" (lines 32-33 in Discussion, 5th paragraph). In what way? Please expand the discussion and provide reference.

8. There are no limitations discussed. Please see my summary comments for some of the limitations of the study and discuss them in discussion section.

Reviewer #5: Please see the attached document with my comments to the authors.

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

Authors' response

Manuscript: Analysis of iodine nutrition level and thyroid function of pregnant women in Yongchuan, Chongqing

Comments to the authors

This study investigated the iodine status and thyroid function of pregnant women in Chongqing, China. The study is not novel, but it adds to existing data on iodine status and thyroid function of pregnant women in China. The manuscript needs extensive English-language editing throughout as in a lot of places the language is unclear and/or grammatically incorrect. There are inaccuracies and missing details throughout. My detailed comments on the content of each manuscript section are included below.

Abstract:

Line 15: The authors should avoid using 'level/s' to refer to the urinary iodine concentration (UIC) and thyroid-hormone concentrations. This is applicable throughout the manuscript.

Response: The 'level/s' in the article have been revised 'concentration/s'.

Line 17: Please add that this is based on the WHO median-UIC criteria for pregnant women.

Response: It has been added in Line 17.

Lines 17- 18: Please avoid saying 'proportion of/with iodine deficiency' as this is not an accurate statement. You could just say 'the proportion below the WHO median-UIC cut-off for pregnant women'. Having a single UIC measurement below the WHO cut-off doesn't necessarily mean that the woman was iodine-deficient, as a single spot-UIC measure is not a marker of individual iodine status.

Response: It has been expressed 'the proportion below the WHO median-UIC cut-off for pregnant women' in the article.

Line 21: Please avoid using 'levels' for FT3 and FT4 concentrations. Please use 'concentration' instead. Response: The 'level/s' in the article have been revised 'concentration/s'.

Lines 28-29: Please use 'concentration' instead of 'levels' when referring to urinary iodine concentration here and throughout the manuscript.

Response: The 'level/s' in the article have been revised 'concentration/s'.

Line 29: 'iodine-appropriate group' is not the widely used term; I think it would be better to use 'iodine sufficient group' or 'group with adequate iodine intake' instead. Please also add the cut-offs used to define this group here.

Response: 'iodine-appropriate group' has been replaced by 'The iodine sufficient group (UIC: 150-249 ug/L)'

Line 30: What are 'the other groups'? Please clarify here.

Response: the other groups represent $UIC \leq 150 \text{ ug/L}$, $UIC 250-499 \text{ ug/L}$ and $UIC \geq 500 \text{ ug/L}$.

Introduction:

Overall, I think the introduction needs more detail to justify the study aim. For instance, what previous data on iodine status and/or thyroid function are available in pregnant women in China and/or in that specific region? How would this study add to the existing evidence? Are there no existing data in pregnant women from this area to guide iodine-supplement use in pregnant women? What are the current recommendations for supplementation?

Response: Since the implementation of salt iodization in 1995, China has basically eliminated iodine deficiency diseases, and some areas have even experienced iodine excess. In 2011, the China Iodine Monitoring Center reported that the median urinary iodine concentration of school-aged children (SAC) was 238.6 ug/L, the goiter prevalence was 2.4%, and the household iodized salt coverage was 98%. Some studies also pointed out that the excessive intake of iodine in China has persisted for 6 years, which has led to dramatic changes in the prevalence and spectrum of thyroid diseases. SAC is a routine group for evaluating iodine nutrition in the community, but adequate iodine intake in SAC does not guarantee iodine sufficiency in pregnant women in the same community. So the urinary iodine level of SAC is not a good indicator for reflecting the iodine nutrition status of pregnant women. In addition, China has a vast territory, people's living habits are very different, and the urine iodine concentration of the population is also different. And there is still no unified view on whether and how to supplement iodine for this special group of pregnant women. At present, there is no research on the iodine nutrition level of pregnant women in Yongchuan area. Therefore, exploring the relationship between thyroid function and iodine level of pregnant women in Yongchuan District is of great significance for clinicians to guide pregnant women to supplement iodine.

Methods:

Line 21: Can the authors provide more detail of how pregnant women were ‘randomly selected’? Response: Sorry, this is the wrong expression. We selected study subjects based on inclusion and exclusion criteria and ensured that there were 100 pregnant women in each group.

Lines 32-41: I think these data on the characteristics of the included women should be moved to the results section.

Response: It has been moved to the results section.

Lines 8- 10: What were the results of the CRMs quality control? Please report here and/or add as supplementary data.

Line 25: According to the WHO criteria, median UIC 250-499 mcg/L refers to more than adequate intake/above requirements, not excessive iodine intake. Please revise this. Response: It has been revised in the article.

Results:

Lines 17- 19: ‘Decrease’ in FT3 and FT4 implies repeated measures within the same woman. This was not the case in this study; you had measures in the three trimesters, but they were from different women. To be clearer, the authors should say ‘higher gestational week was associated with lower FT3 and FT4’ or ‘FT3 and FT4 concentrations were lower in samples from the second/third trimester vs the first’.

Response: It has been expressed ‘The FT3 and FT4 concentrations were higher in samples from the first/second trimester vs the third, the TSH concentration were lower in samples from the first/second trimester vs the third’.

Table 1: Please add what statistical tests were used for these comparisons as a footnote to this table.

Response: It has been added in the article.

Table 2: Is the comparison of UIC between the three trimester groups based on a Chi-square test, as well? If so, that is incorrect; you should report the results of a Kruskal-Wallis test here (since usually UIC is not normally distributed, and you have a continuous variable vs categorical). Please also clarify if the values reported for each UIC group are percentages.

Response: It has been added in the article.

Table 3: What are the statistical tests used to generate these p-values? Please add here as a footnote. Response: It has been added in the article.

Table 4: What are the statistical tests used to generate these p-values? Please add here as a footnote.

Response: It has been added in the article.

Table 5: What were the statistical comparisons done here? It is not clear if

the reported chi-square and p values are from tests comparing total thyroid diseases across the UIC groups. Have you done a chi-square test for each thyroid disease separately across the UIC groups? The authors should clarify this in the table as it is confusing to a reader.

Response: It has been added in the article. p values are from tests comparing total thyroid diseases across the UIC groups.

Figure 1: Are these correlation coefficients based on Pearson's r (i.e., parametric)? UIC is usually positively skewed (i.e., not normally distributed), so I think these should be non-parametric correlations (i.e., Spearman's rho). Please clarify this.

Response: The data has been analyzed by Spearman's rho. The result has been showed in the article.

Discussion:

Lines 14- 16: Please add references to support your statement here.

Response: Businge Charles Bitamazire, Longo-Mbenza Benjamin, Kengne Andre Pascal, Iodine deficiency in pregnancy along a concentration gradient is associated with increased severity of preeclampsia in rural Eastern Cape, South Africa. [J] .BMC Pregnancy Childbirth, 2022, 22: 98. Gargari Soraya Saleh, Fateh Reyhaneh, Bakhshali-Bakhtiari Mina et al. Maternal and neonatal outcomes and determinants of iodine deficiency in third trimester of pregnancy in an iodine sufficient area. [J] .BMC Pregnancy Childbirth, 2020, 20: 174.

Lines 2-5: The authors suggest that iodine deficiency in pregnant women should be detected in the clinic, however, currently there isn't a biomarker of individual iodine status (i.e., over a longer period, not just recent intake in the last 24-48 hours as indicated by a single spot-UIC) that can be used in clinics. UIC from a single spot-urine samples cannot indicate iodine deficiency in an individual and cannot be used to diagnose individuals. This is a big research gap and I think it should be mentioned here, as what the authors suggest is not contextualised to the biomarkers of iodine status currently available to use on an individual basis.

Response: It has been revised in the article.

I have attached the revised article at the end.

Ref.: Ms. No. JCTRes-D-22-00028R1
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Yongchuan, Chongqing
Journal of Clinical and Translational Research

Dear Xiao Zhenghua Xiao,

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For your guidance, reviewers' comments are appended below.

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Your revision is due by Jul 01, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> 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

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Thank you for resubmitting your manuscript to JCTR.

Please note that you have not followed explicit requests in my decision letter:

- 1) provide a manuscript with tracked changes so that we can easily verify the location and depth of implemented changes and their correspondence to what is attested in the rebuttal letter.
- 2) the manuscript is still replete with grammar/spelling/linguistic errors. Please contact the editorial office (m.heger@jctres.com) if you need help contracting a language editing service.
- 3) We asked that "you to address the comment of reviewer 3 and the first comment of reviewer 4 pertaining to spot urinalysis in individuals for the determination of iodine deficiency. We have a serious issue with propagating information that is contrary to clearly established guidelines that in turn are backed by extensive research. Please make sure that this issue is adequately addressed in the revision." The only item that was added in that respect was the phrasing "However, currently there isn't a biomarker of individual iodine status that can be used in clinics. UIC from a single spot-urine samples cannot indicate iodine deficiency

in an individual and cannot be used to diagnose individuals. So in the following research, we should actively search for biomarkers of individual iodine status to provide a basis for individualized guidance of iodine supplementation in pregnant women." This does not constitute an adequate elaboration of the problem.

Furthermore, and building on the previous remark, please explain what the value of your research is when you (correctly) indicate in the discussion that "currently there isn't a biomarker of individual iodine status that can be used in clinics."

Thank you,

Michal Heger
Editor

REVIEWER 2

Please see my comments below:

1) Abstract: this is not properly written. The methods were not described explicitly. English needs to be improved.

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Ma, Z. F. (2020). Iodine nutrition and thyroid function in pregnant women exposed to different iodine sources. *Biological Trace Element Research*, 193(2), 574-575.

4) Results: Please start with the main findings, followed by the secondary findings.

5) The results were poorly written, and did not address the research questions sufficiently.

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Please compare the findings in the study with other published studies. The authors are recommended to include the following references as part of their reference list:

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7) Please improve the English throughout the manuscript.

REVIEWER 3

I see a number of concerns with how the authors present the results, and their suggestion to incorporate urinary iodine testing into routine obstetrics. Urinary iodine concentration is not a good measure of iodine status at the individual level and is recommended for evaluation populations at a group level.

REVIEWER 4

Summary: This is a cross-sectional study of 300 pregnant women from Chongqing, China, assessing urinary iodine levels and thyroid function tests measured in 100 women in each trimester. Strength of the study includes measurement of iodine and thyroid function concurrently in different trimesters. Limitations include cross-sectional study design with single point of laboratory measurements and lack of thyroid antibody assessment. Overall, the findings of this study confirms results of other previous studies regarding association between iodine status and thyroid function in pregnant women. However, the conclusion may be somewhat inappropriate given current limitations in individual-level iodine assessment. Discussion also needs to be expanded.

Specific comments:

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pregnant women or were the same references ranges for non-pregnant adults used for diagnosis of thyroid dysfunction?

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6. "FSH" should be corrected to "TSH" in the first line of the 4th paragraph in discussion (line 8).

7. The authors report "It may be due to the direct effect of iodine on the pituitary and hypothalamus" (lines 32-33 in Discussion, 5th paragraph). In what way? Please expand the discussion and provide reference.

8. There is no limitations discussed. Please see my summary comments for some of the limitations of the study and discuss them in discussion section.

REVIEWER 5

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statement. You could just say 'the proportion below the WHO median-UIC cut-off for pregnant

women'. Having a single UIC measurement below the WHO cut-off doesn't necessarily mean that the woman was iodine-deficient, as a single spot-UIC measure is not a marker of individual iodine status.

Line 21: Please avoid using 'levels' for FT3 and FT4 concentrations. Please use 'concentration' instead.

Lines 28-29: Please use 'concentration' instead of 'levels' when referring to urinary iodine concentration here and throughout the manuscript.

Line 29: 'iodine-appropriate group' is not the widely used term; I think it would be better to use 'iodine sufficient group' or 'group with adequate iodine intake' instead. Please also add the cut-offs used to define this group here.

Line 30: What are 'the other groups'? Please clarify here.

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Overall, I think the introduction needs more detail to justify the study aim. For instance, what previous data on iodine status and/or thyroid function are available in pregnant women in China and/or in that specific region? How would this study add to the existing evidence? Are

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Overall, I think the introduction needs more detail to justify the study aim. For instance, what previous data on iodine status and/or thyroid function are available in pregnant women in China and/or in that specific region? How would this study add to the existing evidence? Are there no existing data in pregnant women from this area to guide iodine-supplement use in pregnant women? What are the current recommendations for supplementation?

Response: Since the implementation of salt iodization in 1995, China has basically eliminated iodine deficiency diseases, and some areas have even experienced iodine excess. In 2011, the China Iodine Monitoring Center reported that the median urinary iodine concentration of school-aged children (SAC) was 238.6ug/L, the goiter prevalence was 2.4%, and the household iodized salt coverage was 98%. Some studies also pointed out that the excessive intake of iodine in China has persisted for 6 years, which has led to dramatic changes in the prevalence and spectrum of thyroid diseases. SAC is a routine group for evaluating iodine

nutrition in the community, but adequate iodine intake in SAC does not guarantee iodine sufficiency in pregnant women in the same community. So the urinary iodine level of SAC is not a good indicator for reflecting the iodine nutrition status of pregnant women. In addition, China has a vast territory, people's living habits are very different, and the urine iodine concentration of the population is also different. And there is still no unified view on whether and how to supplement iodine for this special group of pregnant women. At present, there is no research on the iodine nutrition level of pregnant women in Yongchuan area. Therefore, exploring the relationship between thyroid function and iodine level of pregnant women in Yongchuan District is of great significance for clinicians to guide pregnant women to supplement iodine.

Methods:

Line 21: Can the authors provide more detail of how pregnant women were 'randomly selected'?

Response: Sorry, this is the wrong expression. We selected study subjects based on inclusion and exclusion criteria and ensured that there were 100 pregnant women in each group.

Lines 32-41: I think these data on the characteristics of the included women should be moved to the results section.

Response: It has been moved to the results section.

Line 25: According to the WHO criteria, median UIC 250-499 mcg/L refers to more than adequate intake/above requirements, not excessive iodine intake. Please revise this.

Response: It has been revised in the article.

Results:

Lines 17- 19: 'Decrease' in FT3 and FT4 implies repeated measures within the same woman. This was not the case in this study; you had measures in the three trimesters, but they were from different women. To be clearer, the authors should say 'higher gestational week was associated with lower FT3 and FT4' or 'FT3 and FT4 concentrations were lower in samples from the second/third trimester vs the first'.

Response: It has been expressed 'The FT3 and FT4 concentrations were higher in samples from the first/second trimester vs the third, the TSH concentration were lower in samples from the first/second trimester vs the third'.

Table 1: Please add what statistical tests were used for these comparisons as a footnote to this table.

Response: It has been added in the article.

Table 2: Is the comparison of UIC between the three trimester groups based on a Chi-square test, as well? If so, that is incorrect; you should report the results of a Kruskal-Wallis test here

(since usually UIC is not normally distributed, and you have a continuous variable vs categorical). Please also clarify if the values reported for each UIC group are percentages.

Response: It has been added in the article.

Table 3: What are the statistical tests used to generate these p-values? Please add here as a footnote.

Response: It has been added in the article.

Table 4: What are the statistical tests used to generate these p-values? Please add here as a footnote.

Response: It has been added in the article.

Table 5: What were the statistical comparisons done here? It is not clear if the reported chi-square and p values are from tests comparing total thyroid diseases across the UIC groups. Have you done a chi-square test for each thyroid disease separately across the UIC groups? The authors should clarify this in the table as it is confusing to a reader.

Response: It has been added in the article. p values are from tests comparing total thyroid diseases across the UIC groups.

Figure 1: Are these correlation coefficients based on Pearson's r (i.e., parametric)? UIC is usually positively skewed (i.e., not normally distributed), so I think these should be non-parametric correlations (i.e., Spearman's rho). Please clarify this.

Response: The data has been analyzed by Spearman's rho. The result has been showed in the article.

Discussion:

Lines 14- 16: Please add references to support your statement here.

Response:

Businge Charles Bitamazire, Longo-Mbenza Benjamin, Kengne Andre Pascal, Iodine deficiency in pregnancy along a concentration gradient is associated with increased severity of preeclampsia in rural Eastern Cape, South Africa. [J]. BMC Pregnancy Childbirth, 2022, 22: 98.

Gargari Soraya Saleh, Fateh Reyhaneh, Bakhshali-Bakhtiari Mina et al.
Maternal and neonatal outcomes and determinants of iodine deficiency in third
trimester of pregnancy in an iodine sufficient area. [J]. BMC Pregnancy Childbirth, 2020, 20:
174.

Lines 2-5: The authors suggest that iodine deficiency in pregnant women should be detected in the clinic, however, currently there isn't a biomarker of individual iodine status (i.e., over a longer period, not just recent intake in the last 24-48 hours as indicated by a single spot-UIC) that can be used in clinics. UIC from a single spot-urine samples cannot indicate iodine deficiency in an individual and cannot be used to diagnose individuals. This is a big research gap and I think it should be mentioned here, as what the authors suggest is not contextualised to the biomarkers of iodine status currently available to use on an individual basis.

Response: It has been revised in the article.

I have attached the revised article at the end.

3rd Editorial decision

Ref.: Ms. No. JCTRes-D-22-00028R2

Analysis of iodine nutrition level and thyroid function of pregnant women in

Yongchuan, Chongqing

Journal of Clinical and Translational Research

Dear Xiao Zhenghua Xiao,

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 submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Aug 06, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> 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

Michal Heger

Editor-in-Chief

Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

You have as yet failed to comply with the editor's requests. Consequently, I would like to grant you a final chance to considerably revise the manuscript in accordance with the reviewers' comments.

Please see the attached document that you should use to address EVERY reviewer's comment in a point-by-point manner. Instructions can be found in the journal's author guidelines section (<https://www.jctres.com/en/author-guidelines/>).

Implement changes in your manuscript using the track changes function in Word.

Failure to comply with our requests in revision 3 will lead to a rejection of your manuscript.

Kindest regards,

Michal Heger
EDITOR

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

Authors' response

Please see my comments below:

1) Abstract: this is not properly written. The methods were not described explicitly. English needs to be improved.

The methods has been added. The relevant English expressions have been modified. The revised abstract is as follows:

Abstract Objective Our study reveals the iodine nutrition level and thyroid function of pregnant women in different pregnancy periods in Yongchuan District, Chongqing; investigate the thyroid function dynamics and the incidence of thyroid diseases under different urinary iodine concentrations; evaluate the relationship between iodine nutrition concentration and thyroid function; provide scientific guidance for pregnant women to supplement iodine. **Methods** A total of 300 pregnant women who underwent routine check-ups at the Yongchuan Hospital Affiliated to Chongqing Medical University from January to December 2021 were enrolled. 3ml venous blood and 5ml of clean urine were collected on an empty stomach in the morning. The blood was placed in a general tube containing separating gel, centrifuged at 3000 rpm for 10 minutes to collect serum. The thyroid stimulating hormone (TSH), free thyroxine (FT4) and free triiodothyronine (FT3) were measured by automatic chemiluminescence immunoanalyzer. Urine was placed in a polyethylene plastic test tube, and the urinary iodine concentration (UIC) was detected by WS/T107.1-2016 arsenic-cerium catalytic spectrophotometry. **Results** The overall median urinary iodine concentration of

pregnant women in Yongchuan was 203ug/L. Subgroup analysis were based on gestational weeks, the median urinary iodine concentration in the first trimester group was 187.5ug/L, 211.8ug/L in the second trimester group, and 239.9ug/L in the third trimester group. Based on the WHO median-UIC criteria for pregnant women, all of which were within the sufficient range of iodine. The proportion of below the WHO median-UIC cut-off for pregnant women in the first, second and third trimester is 32%, 30%, and 18% respectively. Compared with the third trimester, the proportion in the early and second trimester was significantly higher, and the difference was statistically significant ($P < 0.05$). The FT3 and FT4 concentrations were higher in samples from the first/second trimester vs the third, the TSH concentration were lower in samples from the first/second trimester vs the third ($P < 0.05$). The TSH concentration gradually increased as the urinary iodine concentration increased. Based on the WHO median-UIC criteria for pregnant women, TSH concentration in iodine deficiency (UIC: < 150 ug/L), more than adequate intake (UIC: 250-499ug/L) and excess iodine (UIC: ≥ 500 ug/L) were significantly different from those in iodine sufficient group (UIC: 150-249ug/l) ($P < 0.05$). The FT3 and FT4 concentrations did not change significantly with urinary iodine concentration ($r_1 = -0.0593$, $P_1 = 0.3053$, $r_2 = -0.0149$, $P_2 = 0.7968$). There was no significant difference in FT3 and FT4 concentrations between different groups ($P > 0.05$). Based on the WHO median-UIC criteria for pregnant women, compared with the iodine sufficient group (UIC: 150-249ug/L), the incidence of total thyroid diseases during pregnancy in iodine deficiency (UIC: < 150 ug/L), more than adequate intake (UIC: 250-499ug/L) and excess iodine (UIC: ≥ 500 ug/L) was significantly increased, and the difference was statistically significant ($P < 0.05$). **Conclusion** The iodine nutrition of pregnant women in Yongchuan District, Chongqing is appropriate, but there are some pregnant women with iodine deficiency or iodine excess. Whether iodine deficiency or iodine excess, the incidence of thyroid disease in pregnant women will increase. In clinical practice, the urine iodine concentration of pregnant women can be dynamically detected at multiple points, which is helpful to correctly guide pregnant women to supplement iodine.

2) Introduction: what is the research gap? The current maternal iodine status in China is not discussed. The authors are recommended to include the following references as part of their reference list:

Ma, Z.F. and Skeaff, S.A., 2017. Assessment of population iodine status. In Iodine deficiency disorders and their elimination (pp. 15-28). Springer, Cham.

Yu, Zengli, et al. "Mild-to-moderate iodine deficiency in a sample of pregnant women and salt iodine concentration from Zhejiang province, China." *Environmental Geochemistry and Health* 42.11 (2020): 3811-3818.

It has been added. It will be showed at introduction of reviewer 5.

3) Methods: the inclusion, exclusion criteria and study protocol were not clearly expressed and logically connected. The authors are recommended to include the following references in their methods as part of their reference list:

Zhou, Hang, et al. "Assessment of iodine status among pregnant women and neonates using neonatal thyrotropin (TSH) in mainland China after the introduction of new revised universal salt iodisation (USI) in 2012: a re-emergence of iodine deficiency?." *International journal of endocrinology* 2019 (2019).

Zhou, Hang, et al. "Iodine deficiency as assessed by neonatal TSH in a sample of mother-and-newborn pairs in Jiangsu Province, China." *Biological Trace Element Research* 199.1 (2021): 70-75.

Ma, Z. F. (2020). Iodine nutrition and thyroid function in pregnant women exposed to different iodine sources. *Biological Trace Element Research*, 193(2), 574-575.

The method has been modified from the above references.

1. Materials and Methods

1.1 Study population and settings: In this study, pregnant women who underwent routine obstetric examinations in Yongchuan Hospital Of Chongqing Medical University from January to December 2021 were selected and grouped according to gestational weeks: first trimester (0-13⁺⁶ weeks), second trimester (14-27⁺⁶ weeks), third trimester (28-40⁺⁶ weeks). Pregnant women were included in the study who were ≥ 18 years of age, lived in the region for ≥ 3 years, had a normal singleton pregnancy and were not diagnosed with thyroid disease^[13]. Pregnant women who developed maternal and neonatal adverse outcomes were excluded from the survey. All data collection was performed at Yongchuan Hospital Of Chongqing Medical University.

Our study had been approved by Ethics Committee of the Yongchuan Hospital Of Chongqing Medical University. All study protocols used in our study were performed according to the Declaration of Helsinki.

4) Results: Please start with the main findings, followed by the secondary findings.

The presentation of all results has been modified as seen in the main text. Reference suggested by the reviewers has been made to the literature.

5) The results were poorly written, and did not address the research questions sufficiently.

The presentation of all results has been modified as seen in the main text.

6) Discussion: Poorly structured, lack of references to the previous study. Please compare the findings in the study with other published studies. The authors are recommended to include the following references as part of their reference list:

Ma, Z. F., & Skeaff, S. A. (2014). Thyroglobulin as a biomarker of iodine deficiency: a review. *Thyroid*, 24(8), 1195-1209.

Zhou, Hang, et al. "Assessment of iodine status among pregnant women and neonates using neonatal thyrotropin (TSH) in mainland China after the introduction of new revised universal salt iodisation (USI) in 2012: a re-emergence of iodine deficiency?." *International journal of endocrinology* 2019 (2019).

Discussion has been revised with reference to the above literature, thanks reviewers. The specific modifications are shown in the text

7) Please improve the English throughout the manuscript.

The editorial office has been contacted for language revisions.

REVIEWER 3

I see a number of concerns with how the authors present the results, and their suggestion to incorporate urinary iodine testing into routine obstetrics. Urinary iodine concentration is not a good measure of iodine status at the individual level and is recommended for evaluation populations at a group level.

There is currently no good measure of iodine status at an individual level. Therefore, we recommend dynamic urinary iodine monitoring for pregnant women, Combined with thyroid function to assess iodine status.

REVIEWER 4

Summary: This is a cross-sectional study of 300 pregnant women from Chongqing, China, assessing urinary iodine levels and thyroid function tests measured in 100 women in each trimester. Strength of the study includes measurement of iodine and thyroid function concurrently in different trimesters. Limitations include cross-sectional study design with single point of laboratory measurements and lack of thyroid antibody assessment. Overall, the findings of this study confirm results of other previous studies regarding association between iodine status and thyroid function in pregnant women. However, the conclusion may be somewhat inappropriate given current limitations in individual-level iodine assessment. Discussion also needs to be expanded.

Specific comments:

1. The conclusion (both in abstract and in discussion) where the authors recommend routine monitoring of urinary iodine levels in pregnant women is currently inappropriate, as there is no good individual level markers of long-term iodine status at this time. As the authors mention in the manuscript, urinary iodine levels are good markers of recent iodine intake and it varies significantly from day to day and depending on food intake. WHO currently recommends median UIC as a marker of population-level iodine status. Therefore, checking spot UIC in pregnant women once may not be adequate to diagnose iodine deficiency or excess.

Therefore, we recommend dynamic urinary iodine monitoring for pregnant women.

2. Was there any Ethics board approval for the study? Please include information regarding Ethics board approval in the manuscript.

Ethics board has approved for the study. It has been modified from the above references.

3. The descriptive results of the demographics of women in each trimester (including table 1) in Materials and Methods section would be more appropriate in Results section.

This has been placed in the results section.

4. Was the thyroid function intervals reported specific for pregnant women? As the authors discuss in discussion, TSH tends to be lower in early pregnancy due to various factors. The reference ranges provided in the materials and methods section appear to be similar to those for non-pregnant adults. Were the reference ranges provided developed specifically for pregnant women or were the same reference ranges for non-pregnant adults used for diagnosis of thyroid dysfunction?

The thyroid function in the report is based on the reference range of the instruments used in the laboratory. And there is currently no reference standard specific to pregnant women in Yongchuan area.

5. What is the environmental iodine level in Chongqing area? My understanding is that water iodine content differs from area to area in China and the difference can be quite significant. This may affect the findings regarding urinary iodine levels in this study, as well as comparison study done in Zhejiang mentioned in discussion (third paragraph).

The discussion in this section has been revised.

Our study evaluated 300 pregnant women at three trimesters. We found that the overall median UIC of the participants overall was 203ug/L. According to the UIC standard of 150-249ug/L recommended by the WHO, is in the range of iodine sufficient. These findings are in line with previous data derived from a larger survey evaluating iodine status in 2607 pregnant Chongqing women[24]. However, compared with studies in Heilongjiang and Hebei province, The UIC in Chongqing was significantly higher^[25-26]. It may be that iodine concentration in household table salt started to drop from 35 mg/kg during 2000–2011 to 20, 25 or 30 mg/kg in 2012 (Chinese Standard GB 26878-2011). Each province is empowered to choose its own iodine content standards. Chongqing chose the highest level of 30 mg/kg. And Heilongjiang and Hebei province are 25mg/kg. This may have affected the UIC. Although the present results suggest that iodine is generally sufficient, we further explored the proportions of different urinary iodine concentrations at three different trimesters. We found that the proportion below the WHO median-UIC cut-off for pregnant women in the 1st, 2nd and 3rd trimester were 32% ,30%, and 18%. Compared with the 3rd trimester, the proportion in the 1st and 2nd trimesters was significantly higher. Which is consistent with Zhang Haihong's findings[27]. It can be explained by the following two reasons. First, due to the pregnancy reaction in the 1st trimester, pregnant women have poor appetite and reduce dietary iodine intake. Some pregnant women are also accompanied by pregnancy vomiting, resulting in increased iodine loss. Second, the fetal thyroid begins to develop at about 10-12 weeks of gestation, and the fetus begins to produce thyroid hormones at 18-20 weeks of pregnancy^[28]. Therefore, in clinical work, iodine nutrition status detection during pregnancy should be carried out as soon as possible, and iodine deficiency should be detected in time, and pregnant women should be reasonably guided to supplement iodine.

6. "FSH" should be corrected to "TSH" in the first line of the 4th paragraph in discussion (line 8)

It has been revised.

7. The authors report "It may be due to the direct effect of iodine on the pituitary and hypothalamus" (lines 32-33 in Discussion, 5th paragraph). In what way? Please expand the discussion and provide reference.

The discussion in this section has been revised. The specific modifications are shown in the text

8. There is no limitations discussed. Please see my summary comments for some of the limitations of the study and discuss them in discussion section.

The limitations of our study include: This study was conducted in a single center only; 2) Postpartum women and neonates were not included in the evaluation; 3) We have a short follow-up period, and observation of pregnancy outcomes and long-term follow-up of offspring have not been completed; 4) The UIC data might not reflect habitual iodine consumption and we do not have data on iodine containing supplement consumption before pregnancy.

In conclusion: Our study adds to a growing body of evidence suggesting that Iodine deficiency or excess iodine can adversely affect the mother's thyroid function. Therefore, we should dynamically monitor iodine status during pregnancy. To provide part of the basis for the decision on whether pregnant women need iodine supplementation.

REVIEWER 5

This study investigated the iodine status and thyroid function of pregnant women in Chongqing, China. The study is not novel, but it adds to existing data on iodine status and thyroid function of pregnant women in China. The manuscript needs extensive English-language editing throughout as in a lot of places the language is unclear and/or grammatically incorrect. There are inaccuracies and missing details throughout. My detailed comments on the content of each manuscript section are included below.

Abstract:

Line 15: The authors should avoid using 'level/s' to refer to the urinary iodine concentration (UIC) and thyroid-hormone concentrations. This is applicable throughout the manuscript.

The 'level/s' has been replaced by 'concentration/s'.

Line 17: Please add that this is based on the WHO median-UIC criteria for pregnant women.

It has been added in the article.

Lines 17-18: Please avoid saying ‘proportion of/with iodine deficiency’ as this is not an accurate statement. You could just say ‘the proportion below the WHO median-UIC cut-off for pregnant women’. Having a single UIC measurement below the WHO cut-off doesn’t necessarily mean that the woman was iodine-deficient, as a single spot-UIC measure is not a marker of individual iodine status.

This has been modified. The proportion of below the WHO median-UIC cut-off for pregnant women in the first, second and third trimester is 32%, 30%, and 18% respectively.

Line 21: Please avoid using ‘levels’ for FT3 and FT4 concentrations. Please use ‘concentration’ instead.

The ‘concentrations’ has been used instead of ‘levels’.

Lines 28-29: Please use ‘concentration’ instead of ‘levels’ when referring to urinary iodine concentration here and throughout the manuscript.

The ‘concentrations’ has been used instead of ‘levels’ in the whole article.

Line 29: ‘iodine-appropriate group’ is not the widely used term; I think it would be better to use ‘iodine sufficient group’ or ‘group with adequate iodine intake’ instead. Please also add the cut-offs used to define this group here.

‘iodine-appropriate group’ has been replaced by ‘iodine sufficient group’.

Line 30: What are ‘the other groups’? Please clarify here.

Based on the WHO median-UIC criteria for pregnant women, compared with the iodine sufficient group (UIC: 150-249 µg/L), the incidence of total thyroid diseases during pregnancy in iodine deficiency (UIC: <150 µg/L), more than adequate intake (UIC: 250-499 µg/L) and excess iodine (UIC: ≥500 µg/L) was significantly increased, and the difference was statistically significant ($P < 0.05$).

Introduction:

Overall, I think the introduction needs more detail to justify the study aim. For instance, what previous data on iodine status and/or thyroid function are available in pregnant women in China and/or in that specific region? How would this study add to the existing evidence? Are there no existing data in pregnant women from this area to guide iodine-supplement use in pregnant women? What are the current recommendations for supplementation?

It has been added.

Pregnancy is a special physiological state. Iodine metabolism and thyroid function are significantly changed compared with those before pregnancy. The physiological requirement

for iodine of pregnant women increases by 50% compared with non-pregnant women. So the risk of pregnant women suffering from iodine deficiency disorders during pregnancy is also significantly increased^[4]. Both iodine deficiency and iodine excess may have irreversible effects on fetal nervous system development and maternal thyroid morphology and function. The United Nations International children's Emergency Fund (UNICEF), the International Council for the control of iodine deficiency disorders (ICCIDD) and the WHO recommend a daily iodine intake of 250ug for pregnant and lactating women^[3,5]. The latest guidelines issued by the American Thyroid Association (ATA) also suggest that women who plan to become pregnant, pregnant or lactating should take oral supplements containing 150ug iodine every day^[6].

Since the implementation of salt iodization in 1995, China has basically eliminated iodine deficiency diseases. In 2011, the China Iodine Monitoring Center reported that the median urinary iodine concentration of school-aged children (SAC) was 238.6ug/L, the goiter prevalence was 2.4%, and the household iodized salt coverage was 98%^[7]. Some studies also pointed out that the excessive intake of iodine in China has persisted for ten years, which has led to dramatic changes in the prevalence and spectrum of thyroid diseases^[8]. SAC is a routine group for evaluating iodine nutrition in the community, but sufficient iodine intake in SAC does not guarantee iodine sufficiency in pregnant women in the same community^[9]. So the urinary iodine concentration of SAC is not a good indicator for reflecting the iodine nutrition status of pregnant women. China has a vast territory, and the concentration of iodized salt varies from region to region. For example, the concentration of iodized salt in Chongqing is 30mg/kg, while that in Zhejiang, Jiangsu is 25mg/kg^[10]. Zengli Yu conducted a cross-sectional study of 625 pregnant women in Zhejiang and found that pregnant women in Zhejiang had mild to moderate iodine deficiency^[11]. Zhao Qingting monitored the iodine nutrition status in Yubei District of Chongqing from 2017 to 2021. The median concentration of urinary iodine in pregnant women in recent five years was in the range of 150.2-249.9ug/L^[12]. However, there is no study on iodine nutrition of pregnant women in Yongchuan area of Chongqing. Therefore, this study aims to explore the thyroid function and iodine nutrition status of pregnant women in Yongchuan District.

Methods:

Line 21: Can the authors provide more detail of how pregnant women were 'randomly selected'?

Sorry, here is the error of expression. In practice, when the group reaches 100 people, the recruitment of the group is stopped.

1.1 General information: A total of 300 pregnant women who underwent routine obstetric examination in Yongchuan Hospital Affiliated to Chongqing Medical University from January to December 2021 were selected.

Lines 32-41: I think these data on the characteristics of the included women should be moved to the results section.

It has been moved to the results section.

Lines 8-10: What were the results of the CRMs quality control? Please report here and/or add as supplementary data.

This has been uploaded to the attachment.

Line 25: According to the WHO criteria, median UIC 250-499 mcg/L refers to more than adequate intake/above requirements, not excessive iodine intake. Please revise this.

It has been revised.

urinary iodine concentration <150ug/L is iodine deficiency, 150-249ug/L is iodine sufficient, 250-499ug/L is more than adequate iodine intake, and ≥ 500 ug/L is iodine excess.

Results:

Lines 17-19: 'Decrease' in FT3 and FT4 implies repeated measures within the same woman. This was not the case in this study; you had measures in the three trimesters, but they were from different women. To be clearer, the authors should say 'higher gestational week was associated with lower FT3 and FT4' or 'FT3 and FT4 concentrations were lower in samples from the second/third trimester vs the first'.

It has been revised.

The FT3 and FT4 concentrations were higher in samples from the 1st/2nd trimester vs the 3rd($P<0.05$). The TSH concentration was lower in samples from the 1st/2nd trimester vs the 3rd($P<0.05$).

Table 1: Please add what statistical tests were used for these comparisons as a footnote to this table.

Footnote has been added under the table.

Table 1 Sociodemographic characteristics of the participants by trimesters

Trimester	N	Age(year)	BMI(kg/m ²)	Pregnancy(n)	Parity(n)
1st	100	30.09 \pm 2.81	21.23 \pm 1.65	1.77 \pm 0.83	0.47 \pm 0.52
2nd	100	29.90 \pm 3.00	21.74 \pm 1.98	1.80 \pm 0.93	0.45 \pm 0.55
3rd	100	30.29 \pm 4.60	21.84 \pm 3.82	1.71 \pm 0.90	0.48 \pm 0.54

P value — 0.240 0.157 0.376 0.868

Data are given as mean±standard deviation

P< 0.05 is statistically significant.

Table 2: Is the comparison of UIC between the three trimester groups based on a Chi-square test, as well? If so, that is incorrect; you should report the results of a Kruskal-Wallis test here (since usually UIC is not normally distributed, and you have a continuous variable vs categorical). Please also clarify if the values reported for each UIC group are percentages.

Footnote has been added under the table.

Table 2 Urinary iodine concentration(UIC) in pregnant women from Yongchuan, Chongqing

Trimester	N	Median(ug/L)	<150(%))	150- 249(%)	250- 499(%)	≥500(%)
1st	100	187.5 ^a	32 ^a	47	10	11
2nd	100	211.8 ^a	30 ^a	46	16	8
3rd	100	239.9	18	48	18	16

Use Kruskal-Wallis test,^aCompared with the 3rd trimester, *P*<0.05

Data are given as median for continuous and % for categorical variables.

Table 3: What are the statistical tests used to generate these p-values? Please add here as a footnote.

Footnote has been added under the table.

Table 3 thyroid function in pregnant women from Yongchuan, Chongqing

Trimester	N	FT3 (pmol/L)	FT4 (pmol/L)	TSH (mU/L)
1st	100	3.11 (1.67- 4.18) ^a	12.5 (7.31- 21.10) ^a	1.45 (0.01- 6.21) ^a
2nd	100	2.77 (0.96- 5.36) ^a	11.5 (7.10- 18.40) ^a	1.88 (0.01- 6.34) ^a
3rd	100	2.57 (0.86- 6.08)	9.19 (0.20- 17.74)	2.27 (0.00- 10.8)

Use Kruskal-Wallis test,^aCompared with the 3rd trimester, *P*<0.05

Data are given as median (min-max).

Table 4: What are the statistical tests used to generate these p-values? Please add here as a footnote.

Footnote has been added under the table.

Table 4 Changes of thyroid function in pregnant women with UIC in pregnant women from Yongchuan,Chongqing

Group	FT3 (pmol/L)	FT4 (pmol/L)	TSH (mU/L)
<150	2.76(1.19-3.99)	11.45(6.46-21.10)	1.45(0.01-6.34) ^a
150-249	2.87 (1.07-6.08)	11.30(7.61-17.74)	1.67(0.01-7.21)
250-499	2.54(0.86-3.78)	10.25(6.41-16.40)	1.87(0.25-10.80) ^a
≥500	2.74(1.23-3.87)	10.80(0.20-12.87)	2.28(0.21-4.35) ^a

Use

Kruskal-Wallis test,^aCompared with the 3rd trimester, $P<0.05$

Data are given as median (min-max).

Table 5: What were the statistical comparisons done here? It is not clear if the reported chi-square and p values are from tests comparing total thyroid diseases across the UIC groups. Have you done a chi square test for each thyroid disease separately across the UIC groups? The authors should clarify this in the table as it is confusing to a reader.

p values are from tests comparing total thyroid diseases across the UIC groups.

Table 5 Incidence of thyroid diseases with different urinary iodine concentrations in pregnant women from Yongchuan, Chongqing

Thyroid diseases	UIC Group			
	<150ug/L	150-249ug/L	250-499ug/L	≥500ug/L
Clinical hypothyroidism	4 (5.00)	1 (0.71)	2 (4.50)	3 (2.86)
Subclinical hypothyroidism	5 (6.25)	1 (0.71)	0 (0.00)	0 (0.00)

Clinical hyperthyroidism	1 (1.25)	0 (0.00)	0 (0.00)	0 (0.00)
Subclinical hyperthyroidism	3 (3.75)	1 (0.71)	0 (0.00)	1 (2.86)
Isolated hypothyroxinemia	18 (22.5)	7 (4.96)	7 (15.91)	5 (14.29)
Total	31 (38.8)	10 (7.10)	9 (22.73)	9 (25.71)
P value	0.000	–	0.011	0.001

Use Chi-square test, Calculate the overall incidence of thyroid disease,

Compared with iodine sufficient group, $P < 0.05$

Data are given as n(%) for categorical variables.

Figure 1: Are these correlation coefficients based on Pearson's r (i.e., parametric)? UIC is usually positively skewed (i.e., not normally distributed), so I think these should be non-parametric correlations (i.e., Spearman's rho). Please clarify this.

these correlation coefficients are based on Spearman's rho. It has been reflected in 1.4.

Discussion:

Lines 14-16: Please add references to support your statement here.

It has been added.

[16] Businge Charles Bitamazire, Longo-Mbenza Benjamin, Kengne Andre Pascal, Iodine deficiency in pregnancy along a concentration gradient is associated with increased severity of preeclampsia in rural Eastern Cape, South Africa. [J]. BMC Pregnancy Childbirth, 2022, 22: 98. doi:10.1186/s12884-021-04356-6.

[17] Gargari Soraya Saleh, Fateh Reyhaneh, Bakhshali-Bakhtiari Mina et al. Maternal and neonatal outcomes and determinants of iodine deficiency in third trimester of pregnancy in an iodine sufficient area. [J]. BMC Pregnancy Childbirth, 2020, 20: 174. doi:10.1186/s12884-020-02863-6.

Lines 2-5: The authors suggest that iodine deficiency in pregnant women should be detected in the clinic, however, currently there isn't a biomarker of individual iodine status (i.e., over a longer period, not just recent intake in the last 24-48 hours as indicated by a single spot-UIC) that can be used in clinics. UIC from a single spot-urine samples cannot indicate iodine deficiency in an individual and cannot be used to diagnose individuals. This is a big research

gap and I think it should be mentioned here, as what the authors suggest is not contextualised to the biomarkers of iodine status currently available to use on an individual basis.

Therefore, we should dynamically monitor iodine status during pregnancy.

REVIEWER 6

1) provide a manuscript with tracked changes so that we can easily verify the location and depth of implemented changes and their correspondence to what is attested in the rebuttal letter.

The modified part of the article has been marked in red.

2) the manuscript is still replete with grammar/spelling/linguistic errors. Please contact the editorial office (m.heger@jctres.com) if you need help contracting a language editing service.

I will contact the editorial office again.

3) We asked that "you to address the comment of reviewer 3 and the first comment of reviewer 4 pertaining to spot urinalysis in individuals for the determination of iodine deficiency. We have a serious issue with propagating information that is contrary to clearly established guidelines that in turn are backed by extensive research. Please make sure that this issue is adequately addressed in the revision." The only item that was added in that respect was the phrasing "However, currently there isn't a biomarker of individual iodine status that can be used in clinics. UIC from a single spot-urine samples cannot indicate iodine deficiency in an individual and cannot be used to diagnose individuals. So in the following research, we should actively search for biomarkers of individual iodine status to provide a basis for individualized guidance of iodine supplementation in pregnant women." This does not constitute an adequate elaboration of the problem.

Furthermore, and building on the previous remark, please explain what the value of your research is when you (correctly) indicate in the discussion that "currently there isn't a biomarker of individual iodine status that can be us

Discussion has been modified.

I have attached the revised article at the end.

The manuscript is still replete with grammar/spelling/linguistic errors.I have contacted the editorial office for language editing services

4th Editorial decision
13-Sept-2022

Ref.: Ms. No. JCTRes-D-22-00028R3
Analysis of iodine nutrition level and thyroid function of pregnant women in
Yongchuan,Chongqing
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: