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OPEN PEER REVIEW

Iron Status and Metabolic Syndrome in Women with Iron Deficiency Anemia: Findings from a Cross-sectional Study in Northern Iran

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

4 comments · 25 Oct 2026 – 1 Nov 2026

Referee 1 Reviewer

ACCEPT 25 Oct 2026

In the conclusion section, indicate what practical applications the results of this study might have in a clinical setting.

Referee 2 Reviewer

MINOR REVISION 27 Oct 2026

1. You defined the cohort by ferritin < 30 and then tested ferritin as the exposure. Isn't the null result simply an artifact of range restriction?
2. You attribute the ferritin difference to inflammation but measured no CRP or hepcidin. On what basis is this interpretation anything more than speculation?
3. Table 3 reports P = 0.040 and P = 0.050 across twelve uncorrected comparisons. What are the stratum sizes and the power, and why present chance-level findings at all?
4. A 32% prevalence from one referral clinic by convenience sampling, with no recruitment flow—how do you justify generalizing this to women with IDA?
5. You claim metabolic abnormalities "could affect" iron markers, which cross-sectional data cannot support. Why were diet, menstrual status, and physical activity never adjusted for?
6. The unadjusted ferritin difference was significant (P = 0.021), yet the abstract says no association. Since BMI is both a MetS component and a mediator, didn't adjusting for it manufacture the null?

Associate Editor

MINOR REVISION 1 Nov 2026

Dear Editor-in-Chief,

In accordance with one of the reviewers' recommendations, the authors should address the requested revisions and submit the revised manuscript before the manuscript can proceed to publication.

Sincerely,
Associate Editor

Editor-in-Chief

MAJOR REVISION 1 Nov 2026

Dear Authors,

Following the evaluation of your manuscript entitled "Iron Status and Metabolic Syndrome in Women with Iron Deficiency Anemia: Findings from a Cross-Sectional Study in Northern Iran" by the reviewer and the editor, you are kindly requested to address the revisions and comments raised by the reviewer and submit the revised manuscript, along with a point-by-point response, to allow further evaluation of your manuscript.

Sincerely,
Editor-in-Chief

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

We would like to thank you for taking the time to review our manuscript. We have taken on board all the suggestions made and have amended the manuscript to improve clarity, methodology and applicability of the study. We have responded to your comments below. During the revision process we double checked the inclusion criteria for our participants. We discovered that one participant did not fully meet the inclusion criteria and so were excluded from analysis. This means the total number of is 196. We have therefore made changes to the descriptive and statistical analysis, tables and sections of the manuscript. We apologize for this mistake but are grateful for the opportunity to improve the accuracy and methodology of the manuscript.

Reviewer 1

Comment: In the conclusion please note the clinical implications of the findings.

- Response:

Thank you for this valid suggestion. We have edited the conclusion to highlight the potential clinical relevance of our findings. Our findings suggest that metabolic syndrome should not be used as an alternative marker for iron status in women with IDA. The assessment of iron status should be performed based on direct measurements of hematological and biochemical parameters including hemoglobin and serum ferritin. Additionally, this highlights the importance of considering metabolic risk factors independently when assessing women with IDA.

Reviewer 2

Comment 1:

Your cohort was defined using ferritin levels (<30) but your exposure was ferritin. Doesn't this mean that your findings are an artefact due to restriction of range?

- Response:

We agree that there is a restriction of range when defining our inclusion criteria based on ferritin levels (<30ng/ml). However, this was a criterion to ensure we had a homogenous cohort with iron deficiency. We have made this clearer in the discussion. We have acknowledged that our findings cannot determine if there is a difference in the relationship between iron stores and metabolic syndrome in those who are not iron deficient, or across the whole range of ferritin levels. Our findings show that we did not find a clear association in this cohort.

Comment 2:

You mentioned that the difference in ferritin was due to inflammation however you didn't measure any inflammatory markers e.g. CRP/hepcidin. How can you be certain this is not just speculation?

- Response:

Thank you for making this point. We agree that we should have been more cautious with our interpretation. As ferritin is an acute phase protein it is possible that inflammatory processes are affecting ferritin. However, we did not measure any inflammatory markers (e.g. CRP/hepcidin). We have made changes to the discussion to ensure we are not directly stating that the difference in ferritin was due to inflammation. We have acknowledged that this may be a possible mechanism. We have also acknowledged this was a limitation of the study.

Comment 3:

In table 3 you have 12 comparisons with P values <0.05 (0.040 & 0.050). How large were your strata and how much power do you have? Why are you even showing significance at the level of chance?

- Response:

We agree that there were several comparisons being made within each group of BMI. There weren't many participants within each category meaning there was a risk of finding significant findings by chance. Additionally, these were not planned analyses. We have removed table 3 and the BMI comparisons. We felt these would not add much to the interpretation of the findings. The new manuscript focuses on the overall data comparing women with/without metabolic syndrome and the regression analysis.

Comment 4:

Your sample was convenience sampled from one referrals clinic. How can you be sure the prevalence is representative of women with IDA?

- Response:

We agree that we cannot infer that the prevalence found in our study is representative of the general population. Our sample was a convenience sample from one referrals clinic meaning there may be issues with selection bias. We have made this clear in the methods section and have acknowledged that the findings may not be representative of the general population in the discussion. Our findings show that 32.0% of women had metabolic syndrome. This figure is specific to our sample. We agree with your comment about the lack of flowchart. We do not have historical data on how many people were screened, we will acknowledge this as a limitation.

Comment 5:

You mention that metabolic abnormalities could affect iron markers however this cannot be supported by cross-sectional data. Why were you never adjusting for diet, menstrual status and physical activity?

- Response:

We agree that we cannot infer causality or temporality with a cross-sectional study. We have made changes to the text to make it clear that we are not saying metabolic abnormalities could affect iron markers. Diet, menstrual status and physical activity were not systematically collected so we couldn't adjust for them. Whilst these variables may affect iron status and metabolic variables they were not collected in this study. This has been acknowledged as a limitation in the discussion.

Comment 6:

There was a significant difference in ferritin when not adjusting for any variables (P=0.021). However, in the abstract you mention there was no association with ferritin due to BMI being part of MetS and a mediator. Wasn't the null finding manufactured by adjusting for BMI?

- Response:

Thank you for pointing this out. We agree that we need to explain the difference between the non-adjusted comparison and regression analysis. In our study there was a slight increase in ferritin in women with metabolic syndrome compared to those. However, this was only a 1 ng/ml difference with lots of overlap between the groups. Additionally, in the non-adjusted logistic regression analysis there was no significant association between ferritin and metabolic syndrome (OR=1.006, P=0.674). Once adjusted for age and BMI there was still no significant association (OR=0.997, 95%CI 0.968-1.026, P=0.836). Therefore, the null finding was not solely due to adjustment for BMI. The significant finding from our comparison shows that there was a difference in ferritin between groups. However, the logistic regression analysis is looking to see if there is an association between ferritin and the odds of having metabolic syndrome. BMI is an interesting factor to consider here. Whilst BMI isn't one of the 5 components of metabolic syndrome according to the NCEP ATP III criteria, it is very closely linked to adiposity and may be associated with metabolic risk and iron biomarkers. Therefore, adjustment for BMI should not be seen as controlling for a confounder.

2 Revision 1

3 comments · 17 Nov 2026 – 17 Nov 2026

Referee 2 Reviewer

ACCEPT 17 Nov 2026

The authors have answered all of my questions and the paper has been greatly improved. Therefore, it can be accepted for publication.

Associate Editor

ACCEPT 17 Nov 2026

Dear Editor-in-Chief,

Following the completion of the peer-review process and careful consideration of the reviewers' comments, I confirm that the manuscript entitled "Iron Status and Metabolic Syndrome in Women with Iron Deficiency Anemia: Findings from a Cross-Sectional Study in Northern Iran" is now considered acceptable for publication.

The manuscript has received favorable evaluations from the reviewers, and no further major scientific or editorial concerns remain.

In my capacity as the handling editor, I recommend that the manuscript be formally accepted for publication. The authors may now be invited to prepare and submit the final version in accordance with the journal's formatting and publication guidelines.

Sincerely,
Associate Editor

Editor-in-Chief

ACCEPT 17 Nov 2026

Dear Authors,

We are pleased to inform you that your manuscript entitled "Iron Status and Metabolic Syndrome in Women with Iron Deficiency Anemia: Findings from a Cross-Sectional Study in Northern Iran" has successfully completed the peer-review process and has been accepted for publication in our journal.

The reviewers have evaluated your manuscript favorably, and the editorial assessment has confirmed its suitability for publication.

We kindly ask you to prepare and submit the final version of your manuscript in accordance with the journal's formatting requirements and author guidelines. Please ensure that all sections, references, tables, figures, and other relevant components are properly formatted before submitting the final files.

We congratulate you on this achievement and thank you for choosing our journal for the publication of your research.

Best regards,
Editor-in-Chief