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OPEN PEER REVIEW

CXCL13 Serum Level as a Potential Biomarker in Vitiligo Patients: Correlation with Disease Activity and Severity

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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

2 comments · 8 Jul 2023 – 8 Jul 2023

Associate Editor

MINOR REVISION 8 Jul 2023

General Comments:
The research article titled "CXCL13 Serum Level as a Potential Biomarker in Vitiligo Patients: Correlation with Disease Activity and Severity" investigates the role of CXCL13 in the etiopathogenesis of vitiligo and its potential as a biomarker for disease activity and severity. The study design is a case-control study, and the authors measured the serum levels of CXCL13 in vitiligo patients and healthy controls. The article provides important insights into the potential involvement of CXCL13 in vitiligo, but there are some areas that could be improved in terms of clarity and presentation.

Introduction:
The introduction provides a good background on vitiligo and its etiopathogenesis. However, it would be helpful to include more specific information about the current understanding of the role of immune dysregulation and autoimmunity in vitiligo. Additionally, while the introduction mentions the association of CXCL13 with other autoimmune and inflammatory diseases, it would be beneficial to briefly explain the role of CXCL13 and its receptor CXCR5 in these diseases and how they might relate to vitiligo.

Methods:
a. Participant Selection and Exclusion Criteria: The article states that patients who had a history of autoimmune conditions, atopy, malignancy, pregnancy, viral infections, or were using immunosuppressive medicines were excluded from the study. It would be helpful to provide more details about how these exclusion criteria were assessed and applied.
b. Data Collection: The article mentions that patients' histories were obtained, including demographic information and medical data. It would be beneficial to specify the specific data collected for each participant, particularly the variables used for correlation analysis.
c. Statistical Analysis: The article briefly mentions the statistical tests used but does not provide specific details about the analysis plan. It would be helpful to mention the specific statistical tests used for each analysis, including the rationale for choosing these tests.

Results:
a. Study Population: The description of the study population should include the ethnic background of the participants, as mentioned in the conclusion section for future studies.
b. Statistical Analysis: The results section mentions the statistical significance of the differences observed but does not provide the effect sizes or confidence intervals. Including effect sizes and confidence intervals would enhance the interpretation of the findings.
c. Correlation Analysis: The results mention that there was no significant correlation between CXCL13 levels and various clinical parameters. It would be helpful to provide the correlation coefficients and their p-values to support this statement.

Conclusion:
The conclusion provides a concise summary of the study's findings. However, it would be beneficial to also mention the potential implications of the findings and the relevance for clinical practice and future research.

Overall, the article provides valuable insights into the potential role of CXCL13 as a biomarker in vitiligo. However, the article would benefit from further improvements in terms of clarity, presentation of results, and linking the findings to the existing literature.

Editor-in-Chief MINOR REVISION 8 Jul 2023

Dear Author,
Thank you for submitting the article. It needs some revision. Please revise it based on the reviewers' and AE's comments.

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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.

Thanks a lot for your kind assessment , I have tried to demonstrate all the points you have kindly addressed .

Reviewers' Comments:

Reviewer 1:

1.Your keywords should be according to MeSH
I have corrected it in the abstract line 19 " **Keywords:** Autoimmune, CXCL13, Vitiligo."

2. Overall, your introduction provides a good overview of the background and rationale for the study. However, I have a few suggestions for improvement:

2. Provide more information about CXCL13 and its role in autoimmune and inflammatory diseases in introduction: While you mention that CXCL13 has been linked to the pathogenesis of various autoimmune and inflammatory diseases, it would be helpful to provide more detail about this and explain how it relates to vitiligo. This could include discussing the mechanisms by which CXCL13 contributes to autoimmune and inflammatory processes and how these mechanisms might be relevant to vitiligo.

Activation of the CXCL13 and its receptor CXCR5 have been linked to the pathogenesis of various autoimmune and inflammatory diseases . Vitiligo is now considered to be an autoimmune disease and CXCL 13 may have a role in vitiligo pathogenesis

I have provided more details about the role of CXCL13 in autoimmune and inflammatory diseases in the introduction " paragraph No 2 "

This study postulates that the role of CXCL13 in vitiligo etiopathogenesis" the mechanism postulated is mentioned in the discussion paragragh No 4"

To the best of our knowledge CXCL13 serum level has not been assessed before in vitiligo patients. So, we aimed to evaluate CXCL13 serum level in patients with vitiligo " paragraph No 4 in the introduction"

3. Clarify the research gap in introduction: While you state that CXCL13 serum level has not been assessed before in vitiligo patients, it is not clear why this is a significant research gap. Providing more context for why this gap exists and what it means for the field would help to clarify the significance of the study.

Because Vitiligo is now considered to be an autoimmune disease and CXCL 13 may have a role in vitiligo pathogenesis as it has a role in other autoimmune diseases

I have provided more details about the role of CXCL13 in autoimmune and inflammatory diseases in the introduction " paragraph No 2

This study postulates that the role of CXCL13 in vitiligo etiopathogenesis" the mechanism postulated is mentioned in the discussion paragragh No 4"

The significance of our study is mentioned in the introduction paragraph No 4

4. Clarify the diagnosis of vitiligo: While you mention that vitiligo was diagnosed based on the clinical evaluation of symmetrically distributed depigmented macules or patches, it would be helpful to provide more detail about the diagnostic criteria used. Were any other diagnostic tests or criteria used to confirm the diagnosis?

Vitiligo was diagnosed, based on the clinical evaluation of symmetrically distributed depigmented macules or patches. On wood's lamp inspection a milky white look supported the diagnosis. Due to the lesions' usual clinical appearance none of the patients had a biopsy "Methods ; paragraph No 2 "

After confirming the diagnosis using the woods lamp , Vitiligo's location, severity, and pattern were evaluated by dermatological examination. The Vitiligo Extent Score was used to gauge the severity of the vitiligo (VES) [7]. Vitiligo Disease Activity (VIDA) score was used to assess the activity of vitiligo Additionally, the disease activity clinical signs such as phenomenon of Koebner's, depigmentation that resembled Confetti, and ill-defined borderlines were assessed in patients.

" Methods ; paragraph No 3 lines 5-13"

5.Provide more context for the study findings: While you mention that the study found a significant difference between serum levels of CXCL13 in patients compared to controls, it would be helpful to provide more context for these findings. For example, what was the magnitude of the difference, and how does this compare to other studies that have measured CXCL13 levels in autoimmune diseases?

In comparison to healthy controls, patients with vitiligo showed significantly higher blood levels of CXCL13 (mean 227.35 ± 125.70 ng/L, range 85.59-538.38 ng/L) **(p=0.002*)** (Figure 1; page No 7)
"statistically significant p value " denoted that CXCL13 could have a role in the pathogenesis of vitiligo
" Results ; paragraph No 2 "

Comparing the results to other autoimmune disease such as SLE : " discussion paragraph no 3 "

> Associate Editor's Comments:

Introduction:

The introduction provides a good background on vitiligo and its etiopathogenesis. However, it would be helpful to include more specific information about the current understanding of the role of immune dysregulation and autoimmunity in vitiligo. Additionally, while the introduction mentions the association of CXCL13 with other autoimmune and inflammatory diseases, it would be beneficial to briefly explain the role of CXCL13 and its receptor CXCR5 in these diseases and how they might relate to vitiligo.

Activation of the CXCL13 and its receptor CXCR5 have been linked to the pathogenesis of various autoimmune and inflammatory diseases . Vitiligo is now considered to be an autoimmune disease and CXCL 13 may have a role in vitiligo pathogenesis

I have provided more details about the role of CXCL13 in autoimmune and inflammatory diseases in the introduction " paragraph No 2 "

This study postulates that the role of CXCL13 in vitiligo etiopathogenesis" the mechanism postulated is mentioned in the discussion paragragh No 4"

To the best of our knowledge CXCL13 serum level has not been assessed before in vitiligo patients. So, we aimed to evaluate CXCL13 serum level in patients with vitiligo " paragraph No 4 in the introduction"

Methods:

a. Participant Selection and Exclusion Criteria: The article states that patients with a history of autoimmune conditions, atopy, malignancy, pregnancy, viral infections, or using immunosuppressive medicines were excluded from the study. It would be helpful to provide more details about how these exclusion criteria were assessed and applied.

The exclusion criteria is based on history from patients " Methods , lines 7-9"

b. Data Collection: The article mentions that patients' histories were obtained, including demographic information and medical data. It would be beneficial to specify the specific data collected for each participant, particularly the variables used for correlation analysis.

demographic information and medical data used " methods ; paragraph No 2 "

c. Statistical Analysis: The article briefly mentions the statistical tests used but does not provide specific details about the analysis plan. It would be helpful to mention the specific statistical tests used for each analysis, including the rationale for choosing these tests.

specific statistical tests used for each analysis, including the rationale for choosing these tests mentioned in the statistical analysis section paragraph No 1 lines "3-6"

Results:

a. Study Population: The description of the study population should include the ethnic background of the participants, as mentioned in the conclusion section for future studies.

I have corrected it in the results section line 1.

b. Statistical Analysis: The results section mentions the statistical significance of the differences observed but does not provide the effect sizes or confidence intervals. Including effect sizes and confidence intervals would enhance the interpretation of the findings.

Yes , I have demonstrated it in the file of "tables revised", table No 2 showing the test of significance

c. Correlation Analysis: The results mention that there was no significant correlation between CXCL13 levels and various clinical parameters. It would be helpful to provide the correlation coefficients and their p-values to support this statement
I have provided the data in the file of " tables revised " table No 3

Conclusion:
The conclusion provides a concise summary of the study's findings. However, it would be beneficial to also mention the potential implications of the findings and the relevance for clinical practice and future research.

CXCL13 serum level was higher in vitiligo patients than those healthy controls, suggesting that it could have a role in the etiopathogenesis of vitiligo. We recommend similar studies with a larger sample size and different ethnic groups, and assessment of tissue expression of CXCL13 in vitiliginous skin.

2 Revision 1

2 comments · 3 Sep 2023 – 3 Sep 2023

Associate Editor

ACCEPT 3 Sep 2023

Dear EIC,
I reviewed the manuscript again. The great effort in improving the manuscript is highly appreciated.
The authors have addressed all comments.
Thank you

Editor-in-Chief

ACCEPT 3 Sep 2023

Dear AUTHOR,
Thank you for paying attention and responding to the reviewer's comments.