

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Association between the neutrophil-to-lymphocyte ratio and psoriasis: A cross-sectional study of the National Health and Nutrition Examination Survey 2011–2014
AUTHORS	Hong, Jiaxin; Lian, Ni; Li, Min

VERSION 1 – REVIEW

REVIEWER	Nguyen , Hao Trong Ho Chi Minh City Hospital of Dermato-Venereology
REVIEW RETURNED	09-Aug-2023

GENERAL COMMENTS	Overall this manuscript is objective and well written. Here are some comments and suggestions for the authors: - "degree of psoriasis" should be replaced with "severity of psoriasis" or "psoriasis severity" - The category of psoriasis as (i) little or no psoriasis, (ii) only a few patches, (iii) scattered patches and (iv) extensive psoriasis could not represent the severity of psoriasis. This should be one of the limitations. - The conclusion "NLR might be accounted as a monitoring tool in management of psoriasis" is not really justified by the results.
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REVIEWER	Kvist-Hansen, Amanda Gentofte Hospital Hud og allergiafdeling, Department of Dermatology and Allergy, Herlev and Gentofte Hospital, Hellerup, Denmark
REVIEW RETURNED	14-Sep-2023

GENERAL COMMENTS	Interesting study that confirms and add new perspectives to existing literature describing an association between psoriasis and the biomarker NLR. The study has a larger sample size than most previous studies investigating the association between the presence and severity of psoriasis and NLR, however a major limitation of this study is the self-reported diagnosis and severity of psoriasis. I have the following comments and suggestions for the authors: 1) In general, the manuscript would benefit from an extensive language edit. 2) The abstract must be revised so it is more precise in the wording. For instance, in line 13 "of whom 238 had a diagnosis of psoriasis" should be changed to "of whom 238 reported a diagnosis of psoriasis" since the information on psoriasis were self-reported. Furthermore, in line 22-23 "Elevated NLR displayed an increase in risk of developing more severe psoriasis ..." should be changed to "Elevated NLR was associated with an increased odds of having more severe psoriasis ...". I do not believe that we from this study
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	<p>can conclude anything about risk of developing psoriasis.</p> <p>3) In the introduction it is written in line 14-15 that “In addition, those with greater psoriasis severity are more susceptible to gastrointestinal discomfort...” I think this is an odd term to use, instead I will suggest “gastrointestinal disease such as inflammatory bowel disease and NFALD” which is what is described in the given reference (Takeshita et al)</p> <p>4) In the results section line 26-27 it is stated that “Elevated NLR value was associated with higher risk of developing more severe psoriasis” again I think this cannot be concluded by the results of this study and therefore I suggest that it is changed to “High NLR values was associated with having more severe psoriasis”.</p> <p>5) In my opinion the most interesting finding of this study is the non-linear association between psoriasis and NLR. Therefore, it could be beneficial for the manuscript with a more in-dept discussion of this finding in terms of the utility of NLR as a biomarker of psoriasis severity and potential cutoff limits.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Hao Trong Nguyen, Ho Chi Minh City Hospital of Dermato-Venereology

Comments to the Author:

1) "degree of psoriasis" should be replaced with "severity of psoriasis" or "psoriasis severity".

Response: We appreciate your suggestion, which helps a lot in the correct presentation of the text. We have replaced "degree of psoriasis" with "severity of psoriasis" or "psoriasis severity" in the manuscript. We have checked the expression of the terminology throughout the manuscript several times, and all of them have been corrected to the correct expression. Again, thank you for pointing out this problem.

2) The category of psoriasis as (i) little or no psoriasis, (ii) only a few patches, (iii) scattered patches and (iv) extensive psoriasis could not represent the severity of psoriasis. This should be one of the limitations.

Response: Thank you for your valuable comments. It was an oversight on our part not to discuss the category of psoriatic lesions as one of the limitations of our study. In clinical practice, commonly used measures for assessing the severity of psoriasis include the Psoriasis Area and Severity Index (PASI) and the Physician Global Assessment (PGA). However, the NHANES database only classifies psoriatic skin lesions into four categories: little or no psoriasis, only a few patches, scattered patches, and extensive psoriasis. Self-reported measures were used instead of structured clinical diagnostic tools to assess psoriasis severity, which might affect the external validity of our results. We acknowledge it as one of the limitations of our study, and we have revised the relevant sentences in the discussion section as follows (Discussion section, page 8):

“Additionally, the extent of psoriatic skin involvement was assessed by questionnaires instead of structured diagnostic scales, such as the Psoriasis Area Severity Index, which might affect the validity of the findings. NHANES categorizes psoriasis as (i) little or no psoriasis, (ii) only a few patches, (iii) scattered patches and (iv) extensive psoriasis, which cannot represent the severity of psoriasis in clinical practice.”

3) The conclusion "NLR might be accounted as a monitoring tool in management of psoriasis" is not really justified by the results.

Response: Thank you for your suggestion. At your suggestion, we have removed this sentence and carefully revised the statement in the conclusion section to make it more rigorous. The revised

conclusions are as follows (Conclusion section, page 9):

“In summary, our study elucidated that the NLR was independently associated with psoriasis and that the association was nonlinear rather than simply linear. We also found evidence in favour of a clear link between the NLR and psoriasis severity. However, further research is warranted to elaborate the detailed mechanism of the NLR in psoriasis.”

Reviewer: 2

Dr. Amanda Kvist-Hansen, Gentofte Hospital Hud og allergiafdeling

Comments to the Author:

1) In general, the manuscript would benefit from an extensive language edit.

Response: Thank you very much for your suggestions. According to the reviewers' comments and suggestions, we have sought the help of native English speakers and professional copyediting to revise the language of this manuscript, and we have also carefully reviewed the language logic several times to make readers have a clearer understanding of our work.

2) The abstract must be revised so it is more precise in the wording. For instance, in line 13 “of whom 238 had a diagnosis of psoriasis” should be changed to “of whom 238 reported a diagnosis of psoriasis” since the information on psoriasis were self-reported. Furthermore, in line 22-23 “Elevated NLR displayed an increase in risk of developing more severe psoriasis ...” should be changed to “Elevated NLR was associated with an increased odds of having more severe psoriasis ...”. I do not believe that we from this study can conclude anything about risk of developing psoriasis.

Response: We appreciate your valuable suggestions, which help a lot to improve the rigor of the paper. We apologize for the imprecise descriptions in our manuscript. Based on your suggestions, we have checked and revised the abstract (Abstract section, page 2).

3) In the introduction it is written in line 14-15 that “In addition, those with greater psoriasis severity are more susceptible to gastrointestinal discomfort...” I think this is an odd term to use, instead I will suggest “gastrointestinal disease such as inflammatory bowel disease and NFALD” which is what is described in the given reference (Takeshita et al)

Response: Thank you for this useful suggestion. We apologize for using inaccurate citation descriptions in the manuscripts. We have thoroughly re-read this reference (Takeshita et al) and made a revised description as follows:

“Numerous studies have suggested associations between psoriasis and other comorbidities, such as gastrointestinal disease, kidney disease, malignancy, and mood disorders.”

4) In the results section line 26-27 it is stated that “Elevated NLR value was associated with higher risk of developing more severe psoriasis” again I think this cannot be concluded by the results of this study and therefore I suggest that it is changed to “High NLR values was associated with having more severe psoriasis”.

Response: We apologize for our oversight, and to prevent similar problems from occurring again, we have double checked the results section. We thank the reviewer for pointing out the inappropriate expression. According to your suggestion, the sentence has been reworded as follows:

“Compared to participants with an $NLR \leq 1.47$ (Q1), those with an $NLR > 2.63$ (Q4) had a significant increase in the odds of “few patches to extensive psoriasis” (Q4 vs. Q1: OR 2.43, 95% CI 1.10–5.36, $P=0.003$). High NLR values were associated with having more severe psoriasis.”

5) In my opinion the most interesting finding of this study is the non-linear association between psoriasis and NLR. Therefore, it could be beneficial for the manuscript with a more in-dept discussion of this finding in terms of the utility of NLR as a biomarker of psoriasis severity and potential cutoff limits.

Response: We thank the reviewer for this insightful comment. In line with this helpful comment, we have provided more details describing the results of the restricted cubic spline analysis, including the

NLR cutoff points when the odds ratio of psoriasis reached its nadir or was equal to 1 (Results section, page 6-7). In addition, we have tried to explain these nonlinear associations in a deeper way in the discussion section (see page 7). Based on the restricted cubic spline plots, our findings indicated a nonlinear correlation between the NLR and the risk of psoriasis. We observed an inflection point in this nonlinear correlation, where the odds ratio of psoriasis decreases before the inflection point and increases thereafter. We also found that NLR levels within a specific range were associated with a lower risk of psoriasis. We have described and discussed the inflection points and curve trends in the revised manuscript. However, we did not further investigate the potential nonlinear relationship between the NLR and psoriasis severity. This was because the NHANES determined psoriasis severity based on patient self-assessment rather than confirmed medical diagnoses or recognized assessment tools like the Psoriasis Area and Severity Index. We acknowledge this limitation and have included it in the discussion section as one of the limitations of our study.

VERSION 2 – REVIEW

REVIEWER	Nguyen , Hao Trong Ho Chi Minh City Hospital of Dermato-Venereology
REVIEW RETURNED	15-Oct-2023
GENERAL COMMENTS	My comments have been addressed. Congratulations to the authors!
REVIEWER	Kvist-Hansen, Amanda Gentofte Hospital Hud og allergiafdeling, Department of Dermatology and Allergy, Herlev and Gentofte Hospital, Hellerup, Denmark
REVIEW RETURNED	27-Oct-2023
GENERAL COMMENTS	The authors have revised the manuscript according to my previous comments, and I think the manuscript is improved. I have no further comments for the authors.