

Dear Editor,

Thank you for your kind handling on our manuscript (53581). We would also like to thank the reviewers for the positive and constructive suggestions made on our manuscript. Following the concerns raised by the reviewers we have made the following changes to our manuscript. The details of the changes made are also included in the response to each comment.

We hope that the revised version will be satisfactory to the reviewers and that it will be recommended for publication in World Journal of Clinical Cases.

Sincerely,

Jian Chen

Reviewer #1: This is an interesting paper on the value of dkk1 and tnf alpha levels for the diagnosis selected do not pose any challenge for the diagnosis of AS, as they do not have low back pain. What is the usefulness of a tool that discriminate patients with a disease with those that by no means could have that disease?. I think that if the authors want to focus in the diagnosis value of this measurements a population that represents a differential diagnosis should have been selected. Also if we are talking about diagnosing AS, this measurements should be able to discriminate AS from no-radiographic Axial SpA, something that is very unlikely.

Response: In this study, we have analyzed the clinical significance of DKK1 and TNF- α in AS (non-radiographic Axial SpA, which we supplemented in the inclusion and exclusion criteria section) and their differential expression in AS patients and healthy people, which is beneficial to define the range of levels of DKK1 and TNF- α in AS and in healthy people. Li et al also adopted similar study design to assess the value of lncRNA-AK001085 in the diagnosis of AS. And the design has the limitations you mentioned above, we will explore the diagnostic value of DKK1 and TNF- α in AS, and hope the more researchers will participate in it.

Li X, Chai W, Zhang G, et al. Down-regulation of lncRNA-AK001085 and its

influences on the diagnosis of ankylosing spondylitis[J]. Medical science monitor: international medical journal of experimental and clinical research, 2017, 23: 11.

2) On the other hand, in the discussion the authors focused on the importance of early diagnosis and they have studied AS, that is not considered an early disease as it already has radiographic damage. It is hard to believe that selecting consecutive patients with AS, the mean disease duration is 1.5 years. Could you please verify and explain how were patients selected to achieve this? I assume that by course of disease you mean disease duration?

Response: In this study, the disease duration of AS patients ranged from 0.1 to 2.6 years. In order to ensure that the patients included in this study are all diagnosed, so many of them are not in the early stage of AS. If the expected results are obtained in this study, a large number of suspected cases will be further analyzed to explore the value of DKK1 and TNF- α in early screening of AS.

3) Under "Difference of DKK-1 expression between the two groups", there is a mistake as it says that hlaB27 correlates and does not correlate with DKK-1 levels.

Response: We were skeptical about this result as well at first, but after several checks, the result remained the same. There are no similar studies for reference, and we will continue to include another group of subjects to figure it out.

4) Related to the same issue, although the correlations between PCR and ESR, IgG and DKK-1 are significant the correlation is very poor ($r=0.1$), this should be considered and discussed.

Response: We have supplemented these results in discussion section.

5) Related to correlations it is not clear if the correlations were only at baseline or after treatment?, please clarify, if they are only before treatment, how was

the correlation after treatment?

Response: We included the expression level of DKK-1 before and after treatment into the same correlation model, and found that DKK-1 was significantly correlated with CRP, IgG, IgM, ESR, BASDAI, and BASMI.

6) There is no mention on how where patients treated. Please include information on current and previous treatments, it is relevant as different treatments might have different effects on TNF and DKK-1 levels.

Response: All patients were treated in Lishui People's Hospital in accordance with according to the guidelines formulated by the American College of Rheumatology, the American Spondylitis Association, and the Spondyloarthritis Research and Treatment Network in 2015. For active AS patients, non-steroidal anti-inflammatory drugs were adopted, if the activity is still high after treatment, tumor necrosis factor inhibitors were used.

7) Curative effect was defined as achieving ASAS 20?. Perhaps the correct term is responders (not curative)

Response: We used the ASAS20 criteria developed by the Assessment in Ankylosing Spondylitis 20% (ASAS20) criteria developed by ASAS International Society to evaluate the efficacy of treatment. An ASAS20 response is defined as improvement of $\geq 20\%$ or at least 10 units of improvement (VAS) as compared with baseline in ≥ 3 of the following 4 domains, with no deterioration (defined as a worsening of $< 20\%$ in the remaining domain:

1. overall VAS of patients
2. VAS for night back pain and total back pain patient
3. Bath Ankylosing Spondylitis Functional Index (BASFI)
4. Inflammation: mean of the severity and duration of morning stiffness (questions 5. and 6 of the BASDAI)

8) How was recurrence defined? please provide a definition.

Response: We have supplemented the recurrence criteria in the Methods section.

9) Why are you in figure 5 correlating a continuous variable with a dichotomous one?. What is the meaning of that? It would be more explicated to compare mean values between them.

Response: We used (mean \pm sd) in results 2.3 and 2.3 to compare the differences between DKK1 and TNF- α before and after treatment.

10) According to figure 5 those patients with lower levels of DKK-1 were the non-responders? and those with high levels of TNF were the non-responders? How do you interpret this feature?

Response: Figure 5 shows the relationship between the levels of DKK1 and TNF- α and the therapeutic effect in AS. The better the treatment therapeutic effect, the higher the DKK1 after treatment, and the lower the TNF- α .

11) As mentioned at the beginning under discussion with this study you could not conclude that dKK1 and TNF measurements are useful for the diagnosis of AS.

Response: As far as we know, this study is the first to analyze the diagnostic value of DKK1 in AS, so we hope that there will be more research to verify our conclusions.

12) Tables and figures should be auto explicated. Please provide the summary measure used(mean, median, %)in each variable of the tables, and complete titles: Univariate and multivariate analysis of what?

Response: We have supplemented the summary measure in title of Table 1 and completed the titles of Tables 4 and 5.

13)In table 1. What do you mean by HLAB27: 75 (i assume that is 75%)before

treatment and 13.27(%?), after treatment? Do you mean that HLAB27 became negative in a large number of patients?. Please clarify

Response: Yes, table 1 shows the number and percentage of HLAB27 positive patients.

Reviewer #2: Minor Comments

1. Table 1 has poor intelligibility and visuality. Change the first row in table 1 For example; study group, before treatment; study group after treatment; control group p-value. Delete χ^2 / t value.

Response: We have deleted χ^2 /t value, but considering that data such as sex remain the same before and after treatment, so we did not divide them into two columns as you suggested.

2. Add the terms before and after for the Tables I and III titles.

Reply: We have added "ROC" in the titles.

3. Table 4 is unnecessary. Please delete. Because your univariate analysis results are not significant.

Response: We have deleted Table 4.

Besides, the peer review process requires 14 to 28 days or longer for each manuscript. Usually, our first decision regarding the pre-acceptance or rejection of a manuscript is based on the comments of one to three reviewers. We will hold a meeting each week to make the first decision of manuscripts. Once the first decision of your manuscript is made, we will notify you immediately by e-mail For the time being your manuscript does not require any changes be made to it before the first decision will be made. You do not need to reply this e-mail, and we request that you await our further contact via e-mail about the decision for acceptance, revision, or rejection
Thank you for your cooperation