

Author Response 2

Response to Reviewers

General answer to the reviewers: Thank you for the careful evaluation and valuable suggestions to our manuscript, "The correlation between Tumor necrosis factor- α and Chronic obstructive pulmonary disease: A Systematic Review and Meta-Analysis" (Manuscript ID TAR-19-034). We carefully read the review comments you have sent us. However, we could not find the reviewers' comments in that letter. Time presses and we revised the manuscript according to the current content of the letter.

Reviewer: 1

Comments to the Author

The authors have clarified most of the comments adequately. However, the discussion needs to be strengthened

For example,

1. Why is only TNF-alpha important in COPD, when there are so many other inflammatory mediators

Answer: TNF-a is one of the important inflammatory factors for COPD, and the importance of other inflammatory factors for COPD can not be ignored. We study TNF-a because it is a controversial factor, and the results of many studies are conflicting.

2. What is the possibility in the future that TNF-alpha levels can be used as a biomarker for COPD severity, COPD exacerbations, COPD progression and mortality.

Answer: In mechanism, on the one hand, during inflammation processes, activated inflammatory cells and a variety of released inflammatory mediators such as IL-8, IL-6, and TNF- α can destroy lung structure and promote the inflammatory response of neutrophils [1]. On the other hand, the elevated blood inflammatory factors might be explained by several previously proposed mechanisms, such as local pulmonary inflammation due to smoking, oxidative stress and tissue hypoxia. Therefore, we can determine the relationship between TNF- α level and the severity of COPD by detecting the level of TNF- α in COPD patients. Some research have reported this [2]. 3. Is it likely that TNF-alpha antagonists may have value in the management of COPD, then it would be useful to study TNF-alpha levels

Answer: Elevated TNF-a is a complication of COPD with infection, such as bacterial or viral infection. TNF-a antagonist also has some effect on COPD treatment, but does not affect TNF-a as a predictor of COPD. On the contrary, the close relationship between TNF-a and COPD is more evident.

4. Whether tissue/BAL TNF-alpha levels have a stronger association with COPD, COPDAE than serum levels of TNF-alpha.

Answer: Thank you for your advice. We have added subgroup analysis based on sample source. As shown in Fig.9 The TNF-a levels have a stronger association with COPD, COPDAE than control group in serum, sputum and BAL.

5. Table 1

The PICOS table should also contain the search strategy terms used for each heading

Answer: We have added search strategy terms for each heading as shown in Table1.

Table 2

6. Table 2. Exclusion standered - meaning not clear

Answer: We have corrected this part in the revised version.

7. Please separate TNF-alpha levels from tissue and BAL studies and serum studies and present them separately. Both of these cannot be compared to each other and need to be analysed separately.

Answer: Thank you for your advice. We have added subgroup analysis based on sample source. As shown in Fig.9 The TNF- α levels have a stronger association with COPD, COPDAE than control group in serum, sputum and BAL.

Reference:

1. Emami Ardestani M, Zaerin O. Role of Serum Interleukin 6, Albumin and C-Reactive Protein in COPD Patients. Tanaffos. 2015; 14(2):134-140.
2. S Singh S, Verma SK, Kumar S, Ahmad MK, Nischal A, et al. Correlation of severity of chronic obstructive pulmonary disease with potential biomarkers. Immunol Lett. 2018,196,1-10.