Reviewer's report

Title: Nitric oxide production in the exhaled air of patients with pulmonary tuberculosis in relation to HIV co-infection

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Reviewer: Mario Malerba

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TITLE : Nitric oxide production in the exhaled air of patients with pulmonary tuberculosis in relation to HIV co-infection

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General comment

This is a controlled study to assess the levels of FeNO and urine nitrate in sputum smear positive tuberculosis patients with and without HIV and to compare it to the levels found on household contacts and healthy blood donors. This because the role of FeNO in the host defence in tuberculosis and HIV infection is still unclear. The authors studied 36 patients with tuberculosis and HIV, 59 patients with tbc and without HIV, 17 household contacts and 46 blood donors and found that Feno levels in patients with tbc (with and without HIV) were lower compared to the values in household and blood donors. However they found an high rate of patients with increased >FeNO levels in TB Hiv- pz (29%), this group of pz had low levels of uNO.

The topic is interesting and this is the first report to my knowledge investigating Feno levels in tbc with and without HIV , however the results have not a clear interpretation .

1- The question of the paper is well defined and the aim of the study is clearly described in the introduction section.
2- The methods applied are appropriate and well described
3- Data are controlled
4- The manuscript now adhere to standards for reporting
5- Discussion is not clear in all sections.
6- Title is clear . The abstract conclusion should be rewritten.
7- The writing is acceptable after revision.

Major Compulsory Revisions

1- FeNO values was found to be reduced in TB/+Hiv and TB/-Hiv groups
compared to other groups. However FeNO values of all the groups studied were within the normal range (5-20 ppb) (see: Reference values for exhaled nitric oxide (reveno) study. Olivieri et al Respiratory Research 2006, 7:94). The authors should discuss this topic in order to make clear if effectively TB with and without Hiv are capable to change pulmonary production of NO.

The Authors replied and discussed satisfactorily

2- In the Discussion it has been hypothesized that low blood levels of l-arginine may be the cause of this reduction, however this important hypothesis has not been furthermore discussed or produced any conclusion. Moreover it should be important to assay l-arginine in HC and BD groups in order to understand the real importance of this theory. Lack of l-arginine dosage in HC and BD groups is an important limitation of the study.

The Authors replied and discussed satisfactorily

3- The importance of uNO values is not clearly explained. There was an unexpected elevation of uNO values in all the groups considered but in TB/-Hiv group. Therefore one can consider “normal” the uNO values found in TB/+Hiv group (because not different when compared to HC and BD groups) and not a sign of an “abnormally” high NO production or an effective immune response. Moreover the relationship between uNO values and the immune response should be supported by other data about immune defence in the subjects studied.

In conclusion the hypothesis reported in the discussion section based on uNO values differences appear to be weak and should be rewritten or deleted.

The authors replied and discussed satisfactorily

4- The conclusions are not supported by the results and should be rewritten. It should be considered that “..decreased NO production in the lung could be a risk factor in acquiring TB..” or could be a consequence of TB infection; the Authors should discuss either the hypothesis.

The conclusions of the paper are well written, but the conclusion of the abstract should be revised

The Authors replied satisfactorily to Minor essential revision

CONCLUSIONS

In my opinion the Authors gave excessive importance to the result of an increased rate of patients with high FeNO levels in Tb Hiv-. This result seems to suggest that in the group of TB Hiv- there are two subgroups one with low Feno Levels and one with High FeNO levels and this remains unexplained. This result should be discussed but could not seriously determine the conclusions of the study.

However the results of this study are interesting and it must be taken in account
the particular population studied.

The conclusions of the study should be based on the results of an unexpected low production of FeNO in the population studied compared to controls (house contacts and blood donors)

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.