Author's response to reviews

Title: Non-Hispanic Whites have higher risk for pulmonary impairment from pulmonary tuberculosis.

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Author's response to reviews: see over
Response to the editor

Title: Non-Hispanic Whites have higher risk for pulmonary impairment from pulmonary tuberculosis.

Editor's comment:

"I think it would be warranted to let the authors know, that at this point in time, they need to provide the information about the extent of lung destruction and hyperinflation (systematic x-ray results) as requested by the second reviewer. Also the information about restrictive versus obstructive impairment of lung function is not clearly described (the first reviewer has to speculate about the grading approach) and the model should be described in detail in the methods section."

Authors’ response:

We agree that clinical correlates to pulmonary function are important to expand. We have done so by adding details on the initial and follow-up chest x-ray of the study patients. These include radiological presentation at initiation of therapy and after 20 weeks of therapy or at the time when the PFT were performed. As expected the chest x-ray scores significantly correlated with PFT (Figure 4 and 6th paragraphs in the results section). This agrees with prior study of similar patients (Thorax 2000;55:32-38).

We have edited the abstract, methods, results and discussion to reflect this additional analysis.

Both the approaches to grading and correlating physical findings are described in an additional paragraph and figures have been added.

“We correlated radiographic abnormality with pulmonary function using a scoring rubric derived from published sources (figure 1) (16). An experienced physician (SEW) read the baseline chest x-rays taken during therapy and follow-up chest x-rays taken after 20 weeks of treatment. Observed abnormalities, cavitation, and infiltration were standardized and scored using the rubric. The summed total score was correlated with observed pulmonary function. “

The results of this correlation are described in a paragraph added beginning at line 200, and in two additional figures:

“We obtained baseline chest x-ray results for 99% of subjects (n=314), and for 90% (n=254) of subjects on after either 20 weeks or at therapy completion. Pulmonary impairment was significantly (p<0.001 ) correlated with the presence and magnitude of abnormal CXR findings for both baseline (Spearman’s rho=0.4), and subsequent readings,(rho=0.42). Figure 4 shows the distribution of a standardized severity index among subjects with pulmonary impairment identified by Spirometry. “
The 2nd reviewer raises important questions regarding adequately describing pulmonary disease phenotypes given the obvious limitations of Spirometry: a tool that has been used for over a century. Pulmonary impairment can be heterogeneous and a wide range of factors has potential to influence PFT findings. Many of these can be difficult to discern or standardize. In this analysis we chose to focus analysis on measurable factors which most plausibly might influence the results, including occupation, body mass index, smoking and race. Our results control for measured risk factors and demonstrated an association between race and pulmonary impairment that is independent of smoking.

We chose not to explicitly label this pulmonary impairment disease phenotype. Even in well studied conditions such as COPD there is little consensus on methods to describe, standardize, or grade the phenotypic diseases.

This manuscript is not designed to or is adequate to show causality. Its primary value is of hypothesis building, as we begin to study and measure health deficits in even successfully treated TB patients. These include functional pulmonary impairment, with a pathophysiological mechanism we do not yet fully understand. In spite of the inherent limitations, this manuscript reports previously unobserved and unsuspected racial and ethnic disparity associated with poor outcomes after tuberculosis treatment.

Again, we want to thank the reviewers and the editor for the insightful comments on our manuscript.