

Authors' reply: Serum Albumin for Tuberculosis in HIV Infected Patients Eligible for Antiretroviral Therapy

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We thank Professor Wiwanitkit for highlighting important aspects of hypoalbuminemia in HIV infected patients.¹ Hypoalbuminaemia can be the result of inadequate protein intake, malabsorption, reduced production in the liver, increased catabolic state or increased excretion of proteins through the kidneys. In patients with chronic diseases such as cancer, tuberculosis or end stage renal disease, hypoalbuminemia can be explained by a reduced protein intake due to anorexia and by an increased catabolic state due to inflammation. However, recent evidence shows that hypoalbuminemia is more likely to be a marker of inflammation than a marker of malnutrition, and nutritional supplementation is unlikely to raise serum albumin levels.²

HIV infection produces chronic inflammation. Hence, HIV could be a cause of hypoalbuminemia and one could expect a correlation between serum albumin concentrations and CD4 cell counts. However, Sudfeld *et al* did not observe an association between serum albumin levels and changes in the CD4 cell counts, and the CD4 cell counts did not affect the value of serum albumin for predicting mortality.³ It is possible that hypoalbuminemia could be a marker of inflammation in HIV infected patients and could be used as a predictor of mortality independent of the CD4 cell count.⁴ Whether the inflammation is produced by HIV itself or by co-infections such as tuberculosis is a matter that deserves further research.

The objective of our study was not to explain the causes of hypoalbuminemia in HIV infected patients, but to explore the usefulness of hypoalbuminemia as a predictor of tuberculosis.⁵ The vast majority of HIV infected patients with tuberculosis are living in low- and middle-income countries, where the smear microscopy of sputum is most of the time the only available highly specific diagnostic test.⁶ In our setting, three-quarters of patients diagnosed with tuberculosis had smear negative sputum.⁷ Even in settings where the Xpert RIF/MTB assay is available, empirical treatment is the rule.^{8,9} Our study suggested that serum albumin could be useful for clinicians working in resource-poor settings when facing smear-negative HIV infected patients with clinical suspicion of tuberculosis. Patients with hypoalbuminemia will be more likely to have tuberculosis. Patients with higher albumin concentrations are less likely to have tuberculosis and,

if they have tuberculosis, they have a better prognosis. The final decision on whether to start anti-tuberculous therapy empirically should not be based solely on the concentration of serum albumin, and other information such as compatible symptoms, physical examination and chest radiography should be taken into account. In Figure 1 we present the hazard ratio and 95% confidence intervals for tuberculosis by serum albumin concentrations using restricted cubic splines (seven knots) and Cox regression. The low cost of the assay and the general availability in health care facilities in resource-poor settings make serum albumin very interesting from a public health point of view. In particular, it could be useful to improve the sensitivity and specificity of the four-symptom screening strategy recommended by the World Health Organization for intensified case finding and isoniazid preventive therapy. However, we agree with Professor Wiwanitkit in that our study has important limitations. It is a retrospective study using routinely collected data in a setting without tuberculosis culture. Only patients who had the serum albumin measured at the time of antiretroviral therapy eligibility were included. Forty-three percent of patients did not have a measurement of the serum albumin and were excluded. Prospective studies are needed to confirm our findings.

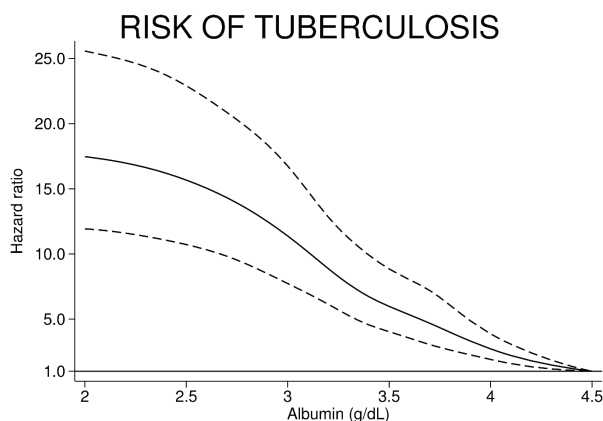


Fig. 1. Risk of tuberculosis within six months (hazard ratio and 95% confidence interval) by serum albumin concentrations of HIV infected patients eligible for antiretroviral therapy

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Ethical issues

There is none to be declared.

Competing interests

The authors declare no conflict of interests.

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