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## CORRESPONDENCE

# Nutritional deficit in miliary tuberculosis: prognostic value

*To the Editors:*

KIM *et al.* [1] have previously shown the prognostic importance of nutritional deficit in the development of acute respiratory failure and further outcome in miliary tuberculosis (MTB). There are a few points that need to be discussed further so that its relevance is properly understood.

Under 4-point Nutritional Risk Score, KIM *et al.* [1] have used severe lymphocytopenia and hypocholesterolaemia as the parameters of poor nutritional status. MTB is characterised by compartmentalisation of lymphocytes at the site of inflammation (lymphocytic alveolitis), leading to their reduced number in peripheral blood [2]. Moreover, total lymphocyte count has not been found to be a suitable marker of malnutrition in the elderly [3]. In addition, keeping the varied presentations and leukocyte counts in MTB in mind, use of severe lymphocytopenia as a parameter does not seem justified.

The role of hypocholesterolaemia as a nutrition status parameter is an area of active research and has not been well proven. Low serum cholesterol levels are also caused by inflammatory mediators during active infection [4] and hence, may not truly depict nutritional deficit. Literature on the association between low serum cholesterol levels and tuberculosis outcome is also lacking.

Malnutrition is the most common cause of immunodeficiency. Nutrition status is a nonspecific parameter that critically determines the outcome of all infections and is not specific to MTB. Animal experiments have shown that malnutrition leads to decreased immunological response to infection, and particularly diminished lymphocyte stimulation and cytokine secretion, leading to poor outcome [5]. Other risk factors, such as presence of meningismus [6], hyponatraemia [7], elevated transaminase levels [8] and adrenal suppression, may specifically predict poor outcome in MTB.

Nutritional deficit has a complex interaction with infection. It not only increases susceptibility to infection but also determines its outcome. Infection may also precipitate nutritional deficiency as in tuberculosis. Initial presentation and severity of miliary tuberculosis may be a better predictor of disease outcome. However, nutritional deficiency can be a confounding factor, and hence should always be looked for and managed along with anti-tubercular therapy in all forms of tuberculosis.

**D. Aggarwal and P.R. Mohapatra**
Dept of Pulmonary Medicine, Government Medical College and Hospital, Chandigarh, Punjab, India.

### STATEMENT OF INTEREST

None declared.

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*To the Editors:*

We read with great interest the recently published informative article by KIM *et al.* [1] on the prognostic value of nutritional deficit in miliary tuberculosis (TB). Using a nutritional risk score comprising of four factors (low body mass index, hypoalbuminaemia, hypocholesterolaemia and severe lymphocytopenia), the authors demonstrated the independent and major prognostic values of nutritional status on both acute respiratory failure and 90-day mortality among 56 patients with miliary TB [1]. However, with the observational nature and retrospective design of the study, it might be difficult to pinpoint the exact cause and effect relationship between nutrition status and TB severity/outcome.

Being underweight is a well known factor that predisposes patients to the development of TB [2, 3]. However, TB may also lead to significant wasting and debilitation [4]. In a large-scale prospective TB treatment trial, being underweight at baseline [5] and the absence of an early gain in weight during chemotherapy have been associated with an increased risk of relapse [6]. As high as 61% of relapsed patients in that trial occurred among those $\geqslant$10% underweight at diagnosis and in turn 62% of these occurred in those failing to gain >5% weight in the initial phase of treatment [5, 6]. However, in the absence of randomised intervention targeted on nutritional status, the question still remains whether the weight gain associated with TB chemotherapy just reflects successful control of the disease, or further augments the host defence against the mycobacterial pathogen.

Miliary TB carries a very substantial degree of mortality. If poor nutritional status does predispose patients to major complication(s) and death, specific intervention targeted at improving the nutritional status would be indicated to decrease the associated morbidity and mortality. Unfortunately, systematically collected data are notably scarce in this area. Notwithstanding that, a cholesterol-rich diet has been shown to accelerate bacteriological sterilisation in pulmonary TB [7]. Micronutrients have also been shown to decrease the risk of reversion of sputum culture to positivity after initial conversion in the first month in both HIV-infected and noninfected patients, but there was no significant effect on mortality [8]. Overall, micronutrients benefitted HIV-uninfected subjects the most in that trial, whereas the opposite was the case in a previous trial in the same locality [9]. Although micronutrient deficiencies often occur in the midst of global nutritional deficits, neither of these trials contained specific information on total protein-calorie intake or serial measurements of body weight or body mass index to allow inference to be drawn on the effect of the overall nutritional status.

Systemic inflammatory responses also appear to play an important role in the development of severe complications in tuberculosis. In the study by KIM *et al.* [1], an elevated C-reactive protein level was also shown to be an independent predictor of acute respiratory failure [1]. Poor appetite and decreased food intake may also be associated with advanced tuberculosis disease. Adjunctive corticosteroid administration during tuberculosis treatment has been found to afford earlier and more significant body weight gain, albeit causes no differences in sputum bacteriological conversion and disease relapse rate [10]. Such a form of treatment might also merit reappraisal in clinical situations associated with heightened inflammatory responses, especially when simple dietary manipulation does not appear to result in a significant improvement in nutrition status.

**C.C. Leung* and W.W. Yew#**

*Tuberculosis and Chest Service, Dept of Health, and #Tuberculosis and Chest Unit, Grantham Hospital, Hong Kong, China.

## STATEMENT OF INTEREST

None declared.

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*To the Editors:*

We have read with great interest the article by KIM *et al.* [1] on the relationship between changes in parameters reflecting nutritional deficit, such as hypocholesterolaemia and prognosis in miliary tuberculosis. We wonder if the value of hypocholesterolaemia in predicting progression to respiratory failure and poor outcome in their patients was not exclusively related to malnutrition (intended as nutritional deficit), but was also related to more severe underlying infection. Indeed, in recent years conventional markers of malnutrition, such as hypocholesterolaemia, have also become recognised as markers of inflammation and severity of illness, for instance in severe infection [2–4]. Curiously, a historical reference for this more recent concept is a 1911 article on febrile tuberculosis [5].

We are involved in using hypocholesterolaemia as a marker of sepsis and severity of illness in critically ill postoperative patients. We often find that sepsis is associated with