Editorial

The link between tuberculosis and body mass index

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Abstract: The evidence behind the strong correlation between reactivation of tuberculosis (TB) and low body mass index (BMI) was reviewed. This strong association between TB and BMI occurred only with pulmonary TB and not extra-pulmonary TB, indicating that a low-BMI body build may in some way predispose to TB reactivation in the lungs. A possible explanation may be the congenital apical lung bullae that occur in 15% of the population and are likely to enlarge in young low-BMI males since biomechanical modeling of pleural stress has shown a massive 40x increase in apical pleural stress in low antero-posterior (AP) diameter chests associated with a low-BMI build. This suggests that pre-existing lung cavities may predispose to TB reactivation instead of current thinking that cavitation occurs after reactivation. Supporting this hypothesis is the relatively common incidence of both TB and primary spontaneous pneumothorax (PSP) occurring simultaneously. Furthermore, this hypothesis also gives a potential explanation for the apical location of secondary TB in the lower lobe as the conventional explanations of high apical oxygen levels and gravity appear to be invalid for the lower lobe. This opens up the possibility of a clinical trial that low-dose computerized tomography (CT) may be used to screen for the presence of subclinical apical bullae in low-BMI, high TB risk cohorts.

Keywords: Tuberculosis (TB); body mass index (BMI); epidemiology

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Tuberculosis (TB) remains a leading cause of mortality worldwide especially in low and medium income states where its incidence is the highest (1) and drug-resistant TB has developed into an escalating problem with serious public health consequences (2,3).

The correlation between body mass index (BMI, the ratio of mass per height squared) and TB was first recognized by Hippocrates (4) and is strongly logarithmic (5). Traditionally it has always been assumed that there is an obvious relationship between nutrition and TB (6). Simply speaking, if one over ate then that person would become obese and the BMI would increase.

TB is also associated with poverty, which in turn drives malnutrition. TB causes children to miss schooling, and in adults, cost of treatment, lack of productivity and stigma of the disease lead to deepening impoverishment. The STOP TB campaign states that *TB fuels poverty and poverty fuels TB* (7,8).

But does low BMI predispose to TB or does it occur after TB infection? To answer this, it is necessary to look at long-term cohort studies that measured BMI before TB infection occurred.

Palmer studied 68,754 US Navy recruits, a study that was extended by Edwards to more than 823,000 Navy recruits. Edwards found that TB developed "three times more often in young men 10% or more below their ideal body weight than in those 10% or more above it" (9,10). Tverdal gathered data from 1.7 million Norwegians with a mean 12.1 years follow up. There was a fivefold increase in age-adjusted incidence of new pulmonary TB in the lowest BMI category as compared to the highest. Tverdal stated that this relationship was a "function of body build" (11). This strong association between TB and BMI occurred only with pulmonary TB and not extra-pulmonary TB (11), indicating

that low BMI somehow only predisposes to TB in the lungs. Comstock suggested that "body build may influence susceptibility to TB because of differences in pulmonary mechanics" (6).

Snider discussed the effect of body build on TB epidemiology in a seminal editorial in 1987 (4). He reported that the evidence that body build influenced TB was long standing. First world war American army soldiers had a higher incidence of TB in tall thin soldiers compared to short and heavyset ones (12). Similar findings were reported in World War II American army soldiers (13). A radiological study of chest radiographs of patients prior to developing TB, with an age/gender/occupation-matched control group, showed that those that developed TB were thinner than the controls (14). Comstock examined the relationship between subcutaneous fat thickness and TB incidence and found that TB prevalence in people with 0–4 mm subcutaneous fat thickness was more than double that in controls with >10 mm fat (15), with active TB infection not related to initial baseline body mass (16). Also, patients with partial gastrectomies for peptic ulcer disease could be stratified for TB risk depending on their pre-operative weight (17).

The strong relationship between active TB and low BMI occurs across varying incidences of TB in different countries and across all levels of BMI (5). This relationship is just the opposite of that occurring in all non-TB respiratory disease; the commonest of which being chronic obstructive pulmonary disease (COPD) and lung cancer; where each 5 kg/m^2 higher BMI is associated with about 20% higher respiratory mortality (18). This means that healthy low BMI patients are at an increased risk of pulmonary TB whilst being protected from other forms of respiratory disease.

Congenital apical lung bullae occur in 15% of the population (19) and are likely to enlarge in young low-BMI males. Biomechanical modeling of pleural stress has shown a massive 40× increase in apical pleural stress in low antero-posterior (AP) diameter chests on coughing (20) that may be expected to stretch any apical bullae. Low-BMI and male gender are associated with a low AP diameter and flattened ribcage shape; also thoracic AP diameter increases with greater age (21).

This means that young, low BMI males are likely to have subclinical enlarging apical bullae that are easy targets for TB reactivation, with the bullae preceding TB infection in this patient cohort, rather than bullae resulting from TB as generally expected. TB reactivation is indeed commonest in the apex of young low-BMI males, as is also primary spontaneous pneumothorax (PSP), a condition characterized by the presence of apical lung bullae. A common pathophysiology of TB and PSP is suggested by the fact that 5.4% of spontaneous pneumothorax patients had TB and 2.1% of patients with TB had PSP (22,23). This hypothesis also gives a potential explanation for the apical location of secondary TB in the lower lobe, whilst the conventional explanations of high apical oxygen levels and gravity for TB's apical localization appear to be invalid for the lower lobe (24).

There is also an association between the human immune response and BMI (25), which can explain the greatly increased risk of TB in HIV co-infected patients (26); however, this leads to more frequent extra-pulmonary TB (27) and does not explain the apical location of pulmonary TB as does the low AP diameter chests associated with a low-BMI build (23).

Low-dose thoracic CT, with a reduced 0.3 mSe radiation exposure instead of the conventional 7 mSe, has been used successfully in lung cancer screening (28). Such CTs, targeted at low-BMI young males with antero-posteriorly flattened chests, may identify the at-risk population with congenital bullae that may be responsible for TB dissemination. However, this would need to be assessed in the setting of a clinical trial in order to evaluate possible effectiveness.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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