

Body Weight Gain in Pulmonary Tuberculosis during Chemotherapy

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Abstract

Background: Wasting is a common feature in tuberculosis and treatment is aimed at achieving weight gain in pulmonary tuberculosis patients. It is believed that weight change after 2 months of intensive phase of treatment can help identify persons at high risk of relapse.

Aim & Objectives: To study the extent of body weight gain in pulmonary tuberculosis during treatment.

Methods/Study Design: This was a retrospective study. Among the patients diagnosed with pulmonary tuberculosis, we included those that were declared clinically cured at the end of 6 months (n=40). Body weights were recorded thrice - at diagnosis (PTB-0), after two months of intensive phase of treatment (PTB-2) and at the end of 6 months of treatment (PTB-6).

Results/Findings: Mean \pm SD of the body weights (in kgs) for PTB-0, PTB-2 and PTB-6 were respectively 41.7 ± 3.79 , 43.13 ± 3.77 and 47.13 ± 3.99 . When compared to PTB-0, PTB-2 and PTB-6 showed higher mean body weights (3.4% and 13% increase respectively). Repeated measures ANOVA of the three test groups showed statistical significance ($p < 0.001$). Tukey HSD post-test between the three groups showed that the means differed significantly from each other ($p < 0.01$ for PTB-0 vs PTB-2, PTB-2 vs PTB-6 and PTB-0 vs PTB-6), indicating that body weight was progressively increasing during the course of treatment.

Conclusion: Treatment of tuberculosis should aim at achieving a higher body weight gain during the intensive phase

Key words: Tuberculosis; Body weight; Chemotherapy

Introduction

Tuberculosis, caused by *Mycobacterium tuberculosis*, still a cause of concern worldwide and is a disease that triggers humoral response in the body.¹ Malnutrition is common among TB patients, with prevalence estimates ranging from 21% in Peru (BMI < 18.5 kg/m²) to 61% in Malawi and 62% in Uganda (BMI < 19.0 in Malawi and Uganda).²⁻⁴ Malnutrition appears to increase the risk of developing tuberculosis, particularly in animal models.⁵ However, cause and effect are difficult to distinguish because tuberculosis disease per se causes weight loss. Most TB patients experience substantial weight gain during TB treatment.^{6,7,8} Reported average weight gain during TB treatment includes 4.9 kg in Indonesia, 5.7 kg in Guinea-Bissau, and 6.9 kg in Tanzania.⁶⁻⁹ However, Kawai and his colleagues found that in their study, patients continued to have low BMI status even after the completion of treatment.¹⁰ According to some authors, body weight generally increases during treatment, but the recovery process is slow and wasting persists for months after the start of antituberculosis therapy.^{11,12} Although increases in body weight and lean tissue usually accompany treatment for tuberculosis, such recovery can be slow and may not be complete, even at the end of the course of tuberculosis therapy.¹²⁻¹⁴ Khan and his team conclude that in the absence of data on other predictors of relapse, weight at diagnosis and weight change after the 2 months of intensive phase treatment can help identify persons at high risk of relapse¹⁵. With these reports in mind, the present study was conducted in a rural hospital in India to study the extent of body weight gain during the intensive as well as continuation phase of anti-tuberculosis treatment.

Materials and Methods

Subjects

This was a retrospective study. Among the patients (25–75 yrs.) who attended as outpatients to The Institute of Thoracic Medicine (ITM), Chennai, India between January 2012 and September 2012 and were diagnosed with pulmonary tuberculosis, those that were new smear positive, who showed sputum conversion at the end of 2 months and were declared clinically cured at the end of 6 months, were included in the study (n=40). The diagnosis of tuberculosis was performed using Ziehl-Neelsen staining method for Acid-fast Microscopy (AFM) and culture for growth of the organism on Lowenstein-Jensen (LJ) medium. PTB patients free from other infectious diseases were included in the study. The patients were also tested for radiographic abnormalities. The study protocol was approved by the Institutional ethics committee and was carried out in accordance with the principle of Declaration of Helsinki.

Labelling of groups

Body weights of all patients were obtained from records and labelled as **PTB-0** (PTB at diagnosis), **PTB-2** (PTB after 2 months of intensive phase of treatment) and **PTB-6** (PTB after 6 months of treatment).

Definition of new smear positive cases

A new patient was defined as a TB patient who has never had treatment for TB or one who has taken anti-TB drugs for less than one month. A smear positive patient was defined as a patient with at least 2 initial sputum smear examinations (direct smear microscopy) positive for acid-fast bacilli (AFB) or a patient with one sputum examination positive for AFB and radiographic abnormalities consistent with active pulmonary TB as determined by the treating Medical Officer (MO) or a patient with one sputum specimen positive for AFB and culture positive for *M. tuberculosis*.

Definition of clinically cured patients

TB patients declared clinically cured included patients who were initially sputum smear-positive patient, who had complied with and completed treatment and had negative sputum smears, on at least two occasions, one of which was at the end of treatment.

Treatment protocol

Treatment was according to the RNTCP-DOTS protocol with the standard recommended dose of the four-drug regimen (Rifampicin, Isoniazid, Pyrazinamide and Streptomycin) in the intensive phase of first 2 months. After confirming sputum conversion, the patients were continued into the next 4 months of continuation phase with the standard recommended dose of the 2 drug regimen (Rifampicin and Isoniazid).

Statistical Analysis

Statistical analysis of the results was carried out using repeated measures ANOVA for comparison between the subgroups (PTB-0, PTB-2 and PTB-6). Following ANOVA for correlated samples, the Tukey HSD posttest was applied to check for significance. To independently assess the effect of the intensive phase of treatment on body weight, the paired t-test was carried out between PTB-0 and PTB-2. For all the tests mentioned, p value of less than 0.05 was considered significant, less than 0.01 very significant and less than 0.001 as extremely significant.

Results

The mean body weights of PTB-0, PTB-2 and PTB-6 were respectively 41.7 ± 3.79 , 43.13 ± 3.77 and 47.13 ± 3.99 . Paired t-test of body weights of PTB-2 with PTB-0 showed significantly higher mean body weight for PTB-2 group ($p < 0.001$) (Figure 1) thus suggesting that 2 months of intensive treatment helped significant body weight gain in the test group. Repeated measures ANOVA of the three test groups (PTB-0, PTB-2 and PTB-6) showed statistical significance ($p < 0.001$). Tukey HSD post-test between the three groups (Table 1) showed that the means of the three groups differed significantly from each other ($p < 0.01$ for PTB-0 vs PTB-2, PTB-2 vs PTB-6 and PTB-0 versus PTB-6), indicating that body weight was significantly progressively increasing during the course of treatment.

Discussion

Current advances in tuberculosis research have drawn the attention of clinicians to focus on body weight gain during treatment to ensure good prognosis, since wasting is recognized not only as a prominent feature of tuberculosis but also as one of the determinants of the disease severity and outcome.¹⁶ Wasting in TB patients may partly be mediated by upregulation of plasma peptide YY with resulting appetite suppression.¹⁷ It is well known that bacterial endotoxins in tuberculosis cause a profound, although transient loss of body weight. The reasons given for this include dehydration caused due to reduced water intake¹⁸ and wasting due to the ‘anabolic block’ or impaired anabolic response to feeding.¹⁹ Weight gain and other improvements in nutritional indicators after effective chemotherapy for tuberculosis have been reported by earlier researchers.^{12,13} In our study, paired t-test of body weights of PTB-2 with PTB-0 showed significantly higher mean body weight for PTB-2 group (3.4% gain, $p < 0.001$) thus showing a significant body weight gain at the end of intensive phase of treatment. Nevertheless, the percentage weight gain was below the desired minimum weight gain (5%) at the end of 2 months. It is to be remembered that a weight gain of 5% or less during the first 2 months of therapy is associated with an increased risk of relapse, even after controlling for other risk factors for relapse.¹⁵ Khan and his team also mention in the same study that it is unclear whether persons are at increased relapse risk if they do not gain weight during 2-month intensive therapy, or whether they are at increased relapse risk because they do not gain weight. They suggest that every effort be made to have underweight patients undergo more than 5% weight gain during the first 2 months of therapy, and/or additional interventions (e.g., extend duration of antituberculosis treatment) be made to decrease relapse risk in underweight patients who do not have greater than 5% weight gain. In the present study, however, it is not yet time to follow-up on the cured patients to check for relapse, if any; because it is only eight months following their completion of treatment.

The mean body weight at the end of 6 months of treatment was still significantly lower than NC in the present study ($p < 0.001$). However, Tukey HSD post-test between the three subgroups showed that the means of the three groups differed significantly from each other ($p < 0.01$ for

PTB-0 vs PTB-2, PTB-2 vs PTB-6 and PTB-0 versus PTB-6), indicating that the decreased body weight at diagnosis was significantly progressively increasing during the course of treatment. When compared to the body weights at diagnosis, there was a 13% body weight gain at the end of 6 months of treatment. Although these findings are encouraging in terms of the efficacy of treatment, earlier researchers have alerted that weight gain during treatment may be mostly due to accumulated fat mass, and patients may fail to restore body protein by the end of treatment²⁰. Accelerating the recovery of lean tissue might help to restore physical function more rapidly. For effective interventions to recover the lean body mass, understanding the body composition of TB patients is important and it needs to be examined in future research.^{21,22} A study conducted by Melchior and his studies showed that in patients with advanced HIV disease and severe wasting has demonstrated the benefits of aggressive nutritional rehabilitation with the use of total parenteral nutrition, which resulted in improved survival.²³ The suggestions of additional intervention for patients with less than 5% weight gain at the end of 2 months of intensive phase of treatment, may be addressed in future studies with randomized controlled trials. Nitrogen balance and protein metabolism studies indicate that patients with tuberculosis can mount a protein anabolic response to feeding.^{11,19,24} Noteworthy suggestions have been made by Jahnvi and Sudha, for warranting further studies in India in order to investigate the impact of nutritional intervention in tuberculosis on socioeconomic and clinical areas, survival, relapse risk, sputum conversion rates, cure rates and death rates.²⁵ We agree with these authors that the Government of India should provide nutritional supplements under the DOTS programme to tuberculosis patients with wasting in the intensive phase of treatment. Nutritional supplementation with culturally appropriate food could prove an effective adjunct therapy for the desired weight gain during the intensive phase of treatment.

Conclusion

Body weight gain during the intensive phase of chemotherapy was less than 5% whereas that during the continuation phase was almost 13% as compared to body weight at diagnosis. Nutritional supplementation under the DOTS programme, with culturally appropriate food could help in improving the rate of body weight gain during the intensive phase of chemotherapy.

Conflict of Interests: The authors stated that there are no conflicts of interest regarding the publication of this article.

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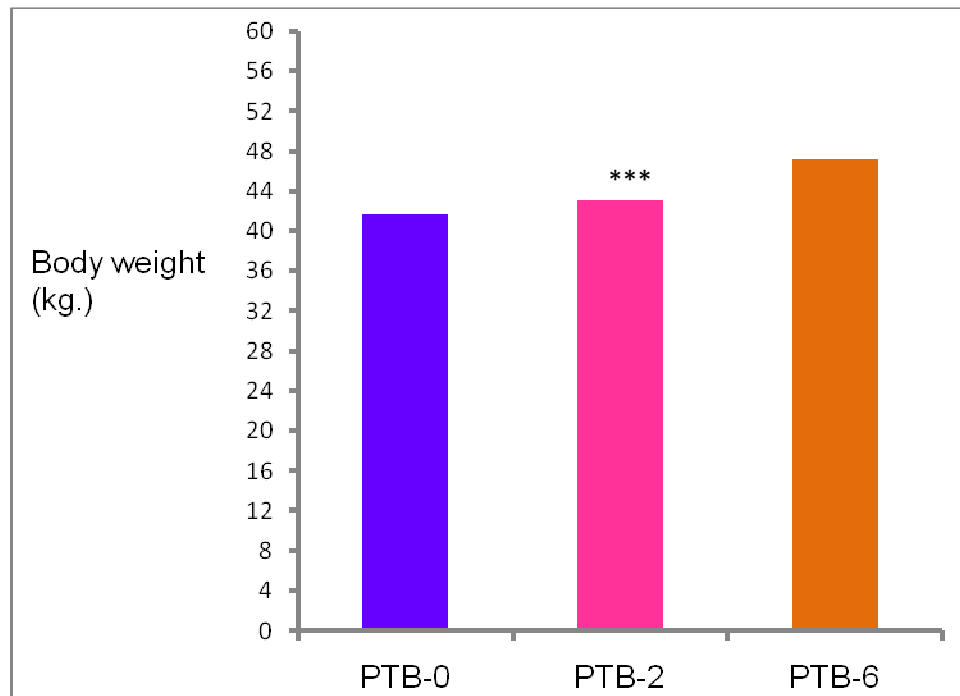


Figure 1: Mean body weight in pulmonary tuberculosis patients at diagnosis, PTB-0 and pulmonary tuberculosis patients at 2 months post treatment (PTB-6). Values are mean \pm SD. (***) $p < 0.001$ for paired t-test vs PTB-0)

Table 1: Results of Tukey HSD post-hoc test between the three subgroups

Parameters	p-values after Tukey HSD post-hoc test		
	PTB-0 vs PTB-2	PTB-2 vs PTB-6	PTB-0 vs PTB-6
Body Weight (Kgs)	<0.01	<0.01	<0.01