Original Research Article

Change in body weight and treatment outcome in sputum positive pulmonary tuberculosis patients treated under directly observed treatment short-course

Malangori A. Parande[1], Pradip S. Borle[1]*, Vinay S. Tapare[1], Sudhakar W. More[2], Susmita S. Bhattacharya[1]

[1]Department of Preventive and Social Medicine, B.J. Govt. Medical College, Pune, Maharashtra, India
[2]State Tuberculosis Training and Demonstration Centre (STDC), Pune, Maharashtra, India

*Correspondence:
Dr. Pradip S. Borle,
E-mail: borlepradip@gmail.com

ABSTRACT

Background: Patients with tuberculosis often suffer from severe weight loss and is used as useful marker to predict TB treatment outcome. Hence a study was planned with an objective to determine the change of patient's body weight over time throughout treatment and to determine whether there was any association with treatment outcome.
Methods: This was a retrospective cohort study, planned to be conducted among all smear positive pulmonary tuberculosis patients registered in a Tuberculosis Unit of Pune corporation, during the period of January to December 2015. Body weights of patients were recorded from TB treatment cards at the time of diagnosis, after 2 months of intensive phase of treatment and at the end of treatment. Total 344 cases were enrolled. Chi-Square test and Fisher's exact test and repeated measure ANOVA test was used for analysis.
Results: A bad outcome was more likely among the category II cases as compared to category I, among non-adherent to treatment cases in continuation phase and higher sputum grading at the time of diagnosis i. e. in 3+ sputum smear grading. The weights of the patients at the time of diagnosis, at end of intensive phase and at end of treatment showed statistical significant difference (p<0.0001). The weight gain, more so at end of treatment was significantly associated with good outcome.
Conclusions: Weight gain has prognostic significance in patients with tuberculosis and should be considered as a surrogate marker to monitor response to TB treatment especially in developing countries where extensive laboratory tests are not feasible.

Keywords: Weight gain after treatment, Sputum smear grading, Tuberculosis, Adherence to treatment

INTRODUCTION

Tuberculosis is the largest single infectious cause of death among young people and adults in the world, accounting for nearly two million deaths per year. The number of deaths yearly in India are 0.11 million; 9% of world mortality. Globally 10.4 million new cases of tuberculosis (TB) occur annually, out of which 2.8 million people are from India alone contributing 27% of the global tuberculosis load.[1] In addition to this, the emergence and spread of multidrug‑resistant TB (MDR‑TB) is threatening to destabilize global TB control.[2] In developing countries like India, undernutrition and TB have a biface relationship. Weight loss or undernutrition is one of the important risk factor for progression of latent TB infection to active TB.[3] At the population level it contributes to an estimated 55% of annual TB incidence in India.[3] Weight loss, wasting and worsening

of nutritional status are important features of TB.[4] Studies on nutritional status of TB patients in India have shown high levels of moderate to severe undernutrition in both women and men.[5,6] According to Revised National Tuberculosis Programme (RNTCP) data, the median weights in men and women are 43 kg and 38 kg, respectively; even lower weights have been documented in patients from rural areas, the poor and marginalized communities.[3] TB patients suffer from weight loss and wasting; since wasting is recognized as a prominent feature of TB but also a major determinant of severity and disease outcome. Malnutrition is one of the most important risk factor for developing TB as it leads to impaired immune system; cell-mediated immunity (CMI) is perhaps the most important among this.[5]

Patients who have lost weight due to TB are expected to gain weight during successful treatment. The association between body weight, TB mortality and morbidity has been studied extensively since 1986.[6,7] Not uncommonly in such studies, weight changes during treatment appeared to be an unreliable and poor indicator of overall treatment response.[8-10] Increased understanding of how patients gain weight during TB treatment in resource poor country such as India may provide an insight into the relationship between TB and malnutrition.

The purpose of this study was to determine the change of patient's body weight over time throughout treatment and to determine whether there was any association with treatment outcome.

METHODS

This was an observational Retrospective cohort study planned to be conducted among all smear positive pulmonary tuberculosis patients who were registered in a Tuberculosis Unit of Pune corporation, Pune selected randomly by lottery method during the period of January 2015 to December 2015. A list of participants during specified period was obtained from tuberculosis register (TB Register) maintained at the tuberculosis unit (TU). The treatment cards of all these patients were filled and kept at the TU, were collected for study purpose. Information about their name, age, sex, address, initial sputum smear result, treatment category, date of start of treatment, co-morbidities, no. of missed doses, reasons for non-adherence, addictions, details of other investigations, sputum smear result during and at the end of their treatment and outcome was collected from the tuberculosis register and treatment cards maintained at the TU. Body weights of all patients were obtained from records at diagnosis, after two months of intensive phase of treatment and at the end of treatment i.e. six months of treatment. Sputum smears were examined for acid fast bacilli (AFB) by Ziehl-Nelsen staining method. The sputum smear results were graded as 1+, 2+ and 3+, scanty and negative as per Revised National Tuberculosis programme guidelines.[11]

The revised definitions given by WHO were used in this study to define the cases and treatment outcomes.[12]

Patients were categorized as follows:

- Cat I- New sputum smear positive

- Cat II- Smear positive relapse, Smear positive failure and Smear positive treatment after default (previously treated)

Patients with negative and scanty sputum were not included in the study.

Ethical considerations

Permission of Institute Ethical Committee was taken. Permission from the City Tuberculosis Officer was taken. As it was record based study, informed consent from the patients was not taken.

Statistical analysis

The data was tabulated and analyzed using SPSS version 23. The data was expressed by calculating percentages and Chi-Square test and Fisher's exact test was used for categorical variable and yate's correction applied whenever necessary and repeated measure ANOVA test for the continuous variable; p value below 0.05 was considered to be statistically significant.

RESULTS

A total of 344 sputum positive patients started antituberculosis treatment during the study period and were eligible for this study. Out of these, 5 patients were not having the weight record at the end of intensive phase and 18 patients were missing the weight record at the end of continuation phase; so were not considered in weight and outcome analysis. Majority of the study subjects 195 (56.7%) were in the age group of 21-40 years and 82 (23.8%) were in 41-60 years age group. The mean age was 35.2 years (SD=14.6; range: 8-78). Male is to female ratio among the study subject was 1:0.6 and 240 (69.8%) were from urban area and 264 (76.7%) belongs to Hindu religion. Majority 185 (53.8%) were working while 159 (46.2%) were unemployed (includes housewives). The number of patients in Category I were 308 (89.5%) and in Category II all patients i.e.36 were of relapse. 324 (94.2%) patients had good outcome which includes cured and treatment completed and 20 (5.8%) had bad outcome which includes failure, death and loss to follow up.

Patient's characteristics with their good and bad outcome were summarized in Table 1. Majority of poor outcome patients were seen in 21-40 years. There were no differences in treatment outcome by age, sex, residence and occupation. A bad outcome was more likely among the category II cases as compared to category I, among

non-adherent cases as compared to adherent (in intensive as well as in continuation phase) and higher sputum grading at the time of diagnosis (in 3+ sputum smear grading) n=11 (18.3%) as compared to 2+ and 1+ sputum n=9 (11.3%).

Table 1: Factors affecting outcome of sputum positive tuberculosis patients.

Factors	Good outcome No. (row%)	Poor outcome No. (row%)	Total No. (column%)	P value
Total	324 (94.2)	20 (5.8)	344 (100)	
Age (years)				
<20	47 (100.0)	0 (0)	47 (13.7)	
21–40	180 (92.3)	15 (7.7)	195 (56.7)	0.231*
41–60	78 (95.1)	4 (4.9)	82 (23.8)	
61–80	19 (95.0)	1 (5.0)	20 (5.8)	
Sex				
Male	196 (93.8)	13 (6.2)	209 (60.7)	0.690*
Female	128 (94.8)	7 (5.2)	135 (39.3)	
Residence				
Urban	225 (93.8)	15 (6.2)	240 (69.8)	0.600*
Rural	99 (95.2)	5 (4.8)	104 (30.2)	
Occupation				
Employed	174 (94.1)	11 (5.9)	185 (53.8)	0.910*
Unemployed	150 (94.3)	9 (5.7)	159 (46.2)	
Category of treatment				
Category I	293 (95.1)	15 (4.9)	308 (89.5)	0.046#
Category II	31 (86.1)	5 (13.9)	36 (10.5)	
Adherence to treatment in intensive phase of treatment				
Missed dose present	52 (86.7)	8 (13.3)	60 (17.4)	0.006*
Missed dose absent	272 (95.8)	12 (4.8)	284 (82.6)	
Adherence to treatment in continuation phase of treatment				
Missed dose present	50 (74.6)	17 (25.4)	67 (19.5)	<0.0001*
Missed dose absent	274 (98.9)	3 (1.1)	277 (80.5)	
Sputum grading at start of treatment				
1+	214 (99.0)	2 (1.0)	216 (62.8)	
2+	61 (89.7)	7 (10.3)	68 (19.8)	<0.0001*
3+	49 (81.7)	11 (18.3)	60 (17.4)	

*- Chi-square test # - Fisher's exact test; P value below 0.05 was considered as statistically significant.

Table 2: Comparison of weight before treatment, at end of intensive and at end of continuation phase in study group.

Phase	N	Weight (Kg)		F value	P value
		Mean	**SD**		
Before start of treatment	326	44.15	8.58		
At end of intensive phase	326	45.71	8.71	406.28	<0.0001
At end of continuation phase	326	48.32	8.88		

Table 3: Association between change in weight at end of intensive period and outcome in study group.

Change in weight at end of intensive period	Good outcome No. (%)	Poor outcome No. (%)	Total No. (%)
Increase in weight	280 (96.6)	10 (3.4)	290 (85.5)
Stable or decrease in weight	44 (89.8)	5 (10.3)	49 (14.5)
Total	324 (95.5)	15 (4.5)	339* (100.0)

Chi-square =4.52, p=0.03; *- out of 344 patients, 5 were missing weight record at end of intensive phase.

The mean body weights of the patient at the start of treatment, at end of intensive phase and at the end of treatment were respectively 44.15±8.58, 45.71±8.71 and 48.32±8.88 (Table 2). Repeated measure ANOVA of

these three groups showed statistical significant difference between the weights of patient (p<0.0001), indicating that body weight was significantly progressively increasing during the course of treatment.

During treatment, at the end of intensive phase (Table 3), majority patients 290 (85.5%) had reported increase in weight and among this group majority 280 (96.6%) had good outcome as compared to the group who had stable

weight or decrease in weight; but this was statistically not significant (p=0.07).

At the end of continuation phase (Table 4), out of 326 patients, 308 (94.5%) had reported increase in weight and had significantly good outcome as compared to the group who had stable weight or decrease in weight (p<0.0001) with OR 30.6 (4.75-197.0) with wide range.

Table 4: Association between change in weight at the end of treatment period and outcome in study group.

Change in weight at the end of treatment period	Good outcome No. (%)	Poor outcome No. (%)	Total No. (%)
Increase in weight	306 (99.3)	2 (0.7)	308 (94.5)
Stable or decrease in weight	15 (83.3)	3 (16.7)	18 (5.5)
Total	321 (98.5)	5 (1.5)	326* (100.0)

Chi-square =28.89, p<0.0001; *- out of 344 patients, 18 were missing weight record at end of treatment.

Table 5: Results of logistic regression showing factors affecting outcome of sputum positive tuberculosis patients.

Factors	Odds ratio (OR)	95% CI for OR	P value
Category of treatment			
Cat I	1	Reference	0.037
Cat II	3.18	1.04-9.75	
Adherence to treatment in intensive phase of treatment			
Missed dose absent	1	Reference	0.181
Missed dose present	2.07	0.82-5.24	
Adherence to treatment in continuation phase of treatment			
Missed dose absent	1	Reference	<0.0001
Missed dose present	31.05	8.77-109.9	
Sputum grading at start of treatment			
1+	1	Reference	<0.0001
2+	12.28	2.49-60.64	
3+	20.02	5.16-111.86	
Weight change at the end of intensive phase			
Weight gain	1	Reference	
Weight stable or decrease	3.18	1.03-9.74	0.04
Weight change at the end of treatment			
Weight gain	1	Reference	<0.0001
Weight stable or decrease	30.6	4.75-197.0	

The results of logistic regression were presented in Table 5. Patients who belong to retreatment (Cat II) category were 3.18 times more at risk of bad outcome as compared to new cases. Missed dose during continuation phase was more important than the intensive phase; were 31.05 times more risk of bad outcome as compared to the patients who were adhered to their treatment. The patients whose sputum is 3+ were 20.02 times more risk of bad outcome. Weight gain at the end of treatment was more important than at end of intensive phase; were 30.6 times more risk of bad outcome as compared to the patients who reported weight loss or stable weight at end of treatment.

DISCUSSION

Tuberculosis is an archetypal wasting disease. Undernutrition is a serious co-morbidity in patients with active TB in India, and increases the risk of severe disease, death, drug toxicity, drug malabsorption and relapse after cure. The DOTS strategy has been found to be very effective all over the world and our country has almost achieved the global target of TB control.[2,13] We evaluated the change in patient's weight throughout treatment and assessed the association between weight change after 2 months intensive phase and at end of treatment and outcome among the sputum positive patients. The mean body weight (in Kgs) of our patients

at the start of treatment was 44.15± 8.58. A study conducted in India was reported similar results of patient's weight at the time of diagnosis while in another study conducted in Peru higher mean patient's weight was reported.[14,15] The change in weight of patients during the treatment duration was statistically significant (p<0.0001) pointing out that change in weight over time is one of the important predictor of treatment outcome in tuberculosis patients. These findings might have an important impact on public health, especially in resource-constrained settings. Weight assessment might be one of the easy, cheap, and useful form to predict TB treatment outcome among patients receiving therapy. Weight gain has been studied for its role as one of the cheaper monitoring tools. Some current guidelines mention that weight loss may indicate incipient treatment failure.[2] Recently, some studies have started to report that weight loss should be considered as clinically relevant.[15,16] One previous study reported that moderate and severe malnutrition was a risk factor associated with early death during TB treatment in rural areas of Malawi.[17] A study in Tanzania conducted among 200 smear-positive pulmonary tuberculosis patients to observe nutritional status found that weight gain during therapy was not a reliable factor to predict treatment outcome but the patients frequently had evidence of malnutrition before and after completion of treatment.[8] In contrast, Krapp et al assessed 650 patients in two health centres in Peru and observed that a body weight gain of <5% was associated with unsuccessful outcome (treatment failures and relapses) at the end of treatment but not after completion of initial phase of treatment.[18] In another study of Malaysia, it was found that weight gain was very common after treatment even though it was not correlated with underlying disease, sputum conversion.[19] Further prospective studies with larger sample size and standardized measurements are needed to corroborate these findings.

Our study has supported other factors associated significantly with outcome in addition to weight gain were category of treatment, adherence to treatment during intensive as well as in continuation phase and sputum grading at the start of treatment. Retreatment cases represent a serious threat to TB control in many settings, and could significantly undermine the overall success of the DOTS strategy; there is less cure rate in such patients and many of them reported failure to gain weight during treatment.[10] TB requires successful completion of at least six or eight months of antituberculosis treatment (ATT).[20] Unfortunately, Anti tuberculosis Treatment compliance is difficult. Missed dose during the therapy represent a threat to weight gain as well as to treatment cure.[20] A high pre-treatment bacillary load appears to be an important predictor for poor treatment outcome and failure to gain weight even under DOTS strategy.

The strength of our study include use of programmatic data in the form of TB treatment cards from a tuberculosis unit to assess body weight change among sputum positive TB patients commencing treatment.

Limitations

This study also had some limitations, like missing data for some of the confounding factors like socioeconomic status of the patient, dietary intake of the patient, addictions, co-morbidities, HIV infection, drug resistance which may influence patient weight and treatment outcome.

CONCLUSION

Weight gain has prognostic significance in patients with tuberculosis and should be considered as a surrogate marker to monitor response to TB treatment especially in developing countries where extensive laboratory tests are not feasible.

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