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Percentage Body Weight Gain During Tuberculosis Treatment: Can It Be a Useful Tool to Predict the Outcome?

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ABSTRACT

Introduction: This present study was conducted to find out usefulness of percentage body weight gain in predicting treatment outcome as well as cut off for successful outcome at different point of time (2 months and 6 months) during treatment.

Methods: In this prospective study 302 tuberculosis patient under treatment were followed up for a period of fifteen months in a North Indian district. Outcome of treatment was assessed at the end of 15 months of follow up. Percentage body weight gain at end of 2nd and 6th month was calculated from the baseline body weight. Data was analyzed using SPSS 20.0. Receiver operating characteristics (ROC) curve was used to find out cut off, sensitivity and specificity for prediction of treatment outcome. All $p < 0.05$ were considered as statistical significant.

Results: 86.8% participants had their treatment outcome successful. Percentage of body weight gain at the end of 2nd and 6th month was found to significantly predict the outcome of treatment. (AUC=0.64 and 0.7, $p < 0.05$). Cut off % body weight gain were ≥2.5 % and ≥ 6.4% at the end of 2 months and 6 months respectively to predict successful outcome.

Conclusion: Percentage body weight gain was found to be a useful predictor of tuberculosis treatment outcome.

Keywords: Body weight gain, tuberculosis, treatment outcome, prediction

INTRODUCTION

Globally, Tuberculosis claims a million of lives every year that includes more than one fifth from India.[1] The duration of treatment of this killer disease is more than half of a year. There are numerous threats to the successful completion of treatment in term of loss to follow up, failure, drug resistance and death.[2] If these aforesaid unsuccessful outcomes can be predicted, appropriate action can be taken at the right time. Sputum conversion and body weight gain are being used in monitoring the treatment response of TB by Revised National Tuberculosis Control Program (RNTCP), India.[2] Monitoring Sputum Conversion is predominantly for sputum smear positive TB cases.[3] Though body weight gain is an established outcome predictor of treatment,[4–7] in the absence of evidence based national or regional cut off in predicting results, its usage has been undermined in the program. There is a bidirectional relationship between nutrition and tuberculosis i.e. malnutrition itself is a risk factor for TB and the diseases causes wasting in the affected individuals.[8,9] Thus effective treatment of TB always shows body weight gain of patients in various national and international studies.[5,6,10,11] In recent past various efforts were made to establish relationship between body weight gain during tuberculosis treatment and outcome, but very few longitudinal studies have been conducted to find out cut off at different point of the treatment.[12,13]

We couldn't find any work on this topic in India where TB has been persisting as a major public health problem and has been targeted for elimination before 2030.[14]

Therefore, this study was conducted to evaluate the usefulness of percentage of body weight gain in predicting outcome and also to find out cut off at different point of time (2months and 6 months) among TB patients under treatment in a district in North India.

METHODS

This prospective study was conducted in a district of western Uttar Pradesh, India from April 2012 to June 2013. Revised National Tuberculosis Control Programme (RNTCP) covered entire population of the district through 7 tuberculosis units (TU). The programme was implemented through 32 designated microscopy centres (DMC) under these tuberculosis units. All the patients aged more than 15 years, registered under Directly Observed Treatment Short course in four designated microscopy centres from April to June 2012 were included in this study. Total 302 tuberculosis patients aged 15 years or more were considered for this study.

All eligible participants were treated under supervision of Directly observed treatment (DOT) providers as per RNTCP guideline. Socio demographic characteristics like age, sex, marital status, education, occupation, residence, standard of living index; personal habits such as smoking and alcoholism and information regarding disease such as, site of infection, type of case, sputum status were captured using a semi structured questionnaire at the initiation of treatment. Weight of the study participants over the treatment period at different point of times (baseline, at the end of 2 months and 6 months) were measured using standard methodology.[15] Weight was measured in the upright position with minimal possible clothing to the nearest 0.1 kg using calibrated SECA weighing balance. This tool was standardised with another weighing machine. Outcome of treatment were recorded at least after one year of follow up. Those patients who "completed their full course with in the stipulated period (treatment completed)" and/or "converted in to sputum negative after five months of treatment on at least 2 occasions (Cured)" were considered as successful outcome. Those patients who died or lost to follow up treatment (default) or continued to be sputum positive for Acid fast bacilli (AFB) after 5 months of treatment (failure) were considered as unsuccessful outcome.[16]

Data was entered and analysed in Statistical Product and Service Solutions [IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.]. IBM SPSS statistics was used for analysis through the academic research facilities provided by the Aligarh Muslim University, Uttar Pradesh. Categorical variables like sociodemographic characteristics, disease related characteristics and outcome of treatment (Successful/un successful) were tabulated as frequency and percentage. Weight (in Kg) was calculated for the participants as mean and standard deviation at different points of time and comparison at 3 time points was carried out using repeated-measures ANOVA in general linear models with time (months 0, 2, and 6 months). Percentage of body weight gain was calculated for end of 2 months and 6 months compared to baseline weight. Percentage of weight gain in the successful and unsuccessful outcome groups was compared using box-whisker plot. Receiver-Operating characteristics (ROC) curve were performed to find out sensitivity and specificity for percentage of body weight gain in predicting successful outcome at two different point of treatment i.e. at 2 months and 6 months. Area under curve and 95% confidence Interval were reported to find out the appropriateness of prediction model. All *p*-values were two-sided, with $p < 0.05$ considered statistically significant. This study was approved by institute ethics committee of JN Medical College, Aligarh. Prior permission was taken from district tuberculosis authority. Informed consent was taken from all adult patients and assent was taken from the parents of aged less than 18 years.

RESULTS

A total of 302 tuberculosis patients were included in the present study. Out of them 18 participants were excluded in body weight analysis after 2 months on account of loss to follow up. Further 10 patients were lost to follow up at the end of 6 months. The age of the participants ranged from 15 to 75 years with mean of 36 ± 15.4 years. Majority were male (72.2 %) and residing in urban area (53%). More than one third was illiterate. Around 21% were having low standard of living index. More than half of the study participants were current or previous smoker and 12.6% were using alcohol as per the study finding. (Table 1)

More than 80% participants were under treatment for pulmonary tuberculosis. Out of 302 study participants, 86.4% were new cases thus having category I treatment under DOTS. At the baseline, three of every five participants had nutritional status as underweight i.e. body mass index below 18.5 kg/m^2. (Table 1) After 15 months of follow up, 86.8% (262/302) achieved successful outcome while unsuccessful outcome was detected in rest of the 13.2% in term of death or treatment failure or default. (Table 2)

Table 1: Socio demographic and baseline characteristic of study participants (n=302)

Variables	Participants (%)
Age group (yrs)	
15-30	131 (43.4)
31-45	90 (29.8)
46-60	57 (18.9)
>60	24 (7.9)
Male Gender	218 (72.2)
Urban Residence	161 (53.0)
Illiterate	110 (36.4)
Standard of living index	
Low	65 (21.5)
Medium	100 (33.1)
High	137 (45.4)
Smoker	156 (51.7)
Alcoholics	38 (12.6)
Pulmonary TB	244 (80.8)
New (Category-I) Treatment	261 (86.4)
Under weight	183 (60.6)

Table 2: Distribution of cases according to outcome of treatment (n=302)

Outcome	Frequency	Percent
Successful	262	86.8
Unsuccessful	40	13.2

Table 3: Comparison of body weight at baseline, 2months and 6 months of treatment

Weight (kg)	Mean (kg)	SD (kg)
Baseline (n=302)	46.01	6.4
After 2 months (n=284)	47.94	6.2
After 6 months (n=274)	50.03	6.5
Increase in weight in 2 months (n=284)	1.9	0.62
Increase in weight in 6 months (n=274)	4.0	0.75

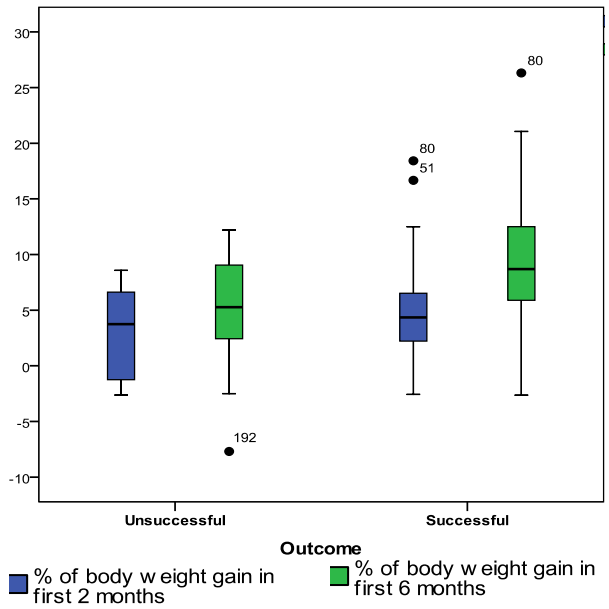

Figure 1: % Body Weight Gain across treatment outcomes and treatment period

Table 3 summarizes body weight profile of the study participants at baseline and two point of follow up (at the end of 2nd and 6th months). At the initiation of treatment, mean body weight was 46 ± 6.4 kg with a range from 31 to 65 kg. At the end of 2 months i.e. after Initiation Phase (IP) mean body weight was 47.94±6.2 kg with a mean increment of 1.9±0.62 kg. Out of the 284 participants at the end of 2 months, 38 (13.4%) did not witness any weight gain rather weight loss was observed in 11 (4%) cases. Half of the participants gained more than 2 kg at the end of intensive phase and another one fourth achieved same at the end of the 6 months. Mean body weight was 50±6.5 kg at the 2nd point of follow up i.e. end of 6 months. A mean body weight gain of 4.0±2.0 kg was observed in comparison to baseline at this point.

A significant augmentation of body weight noticed among the participants with repeated measure ANOVA followed by bonferroni post hoc test. The difference was statistically significant ($p<0.05$)

Amongst participants with successful and unsuccessful outcome, % body weight gain ranged from – 2.6kg to 8.5kg and -2.5kg to 18kg, respectively. Only half of unsuccessful outcome patients had achieved 2% body weight gain at the end of 2 months while it was 4.3% for treatment successful group. Median percent body weight gain was 5.2 %and 8.6 % at the end of 6 months among the two outcome groups. (Unsuccessful vs Successful) (Figure 1) ROC curves depicts that % body weight gain at the end of 2nd and 6th month significantly predicts the outcome of treatment. (Area Under Curve-0.64 and 0.7, $p < 0.05$). Figure 3 depicts determination of treatment outcome. The cut off was found to be 2.5 % and 6.4% for predicting treatment outcome with sensitivity (70% & 71%) and specificity (64% and 70%) (figure 2 a&b) (Table 4).

DISCUSSION

In this study we evaluated whether percentage body weight gain could be useful for predicting treatment outcome of tuberculosis patients on DOTS. Body weight gain compared to basal weight was longitudinally followed up to end of 6 months. This study showed that patients with successful outcome witnessed approximately twice the increased in % body weight gain compared to unsuccessful outcome. Similar weight gain trend was seen in first 2 months and last 4 months in the both the groups. Slower gain in first 2 months of unsuccessful outcome group was carried forward in the last 4 months, while comparatively faster growth was seen in successful outcome group. There was overall significant increase in bodyweight throughout the tuberculosis treatment.

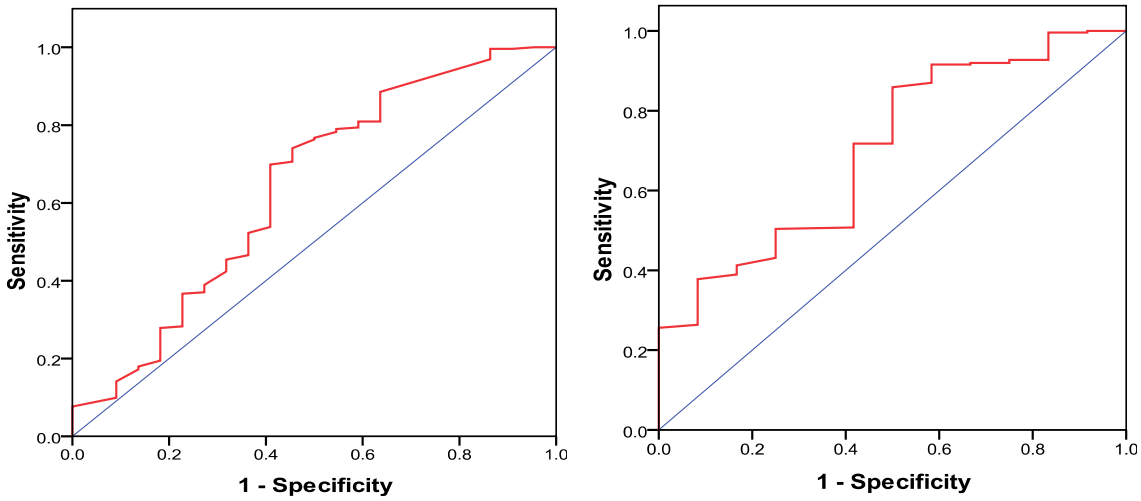

Figure 2 a&b : ROC curve distribution of % body weight gain in predicting successful treatment outcome at the end of 2 months (a) and at the end of 6 months treatment (b)

Table 4: Sensitivity, Specificity, cut off and area under curve

ROC	Cut off (%)	Sensitivity (%)	Specificity (%)	Area under Curve	p value
Body weight gain in 2 months	2.5	70	59.3	0.64	0.032
Body weight gain in 6 months	6.4	71.8	60	0.7	0.018

Mean body weight was increased by 2 kg in first 2 months and further 2 kg in next four months. This shows that the gain in body weight was more rapid in first two months of treatment. This is in coherence with the fact that bacterial load decreases more in intensive phase of treatment.[17] This indicates that DOTS decreased the bacterial load and was effective in treatment. This study highlights that changes in body weight gain can be used to predict the tuberculosis treatment outcome at the end of the treatment. It shows that an increase in ≥2.5% of basal body weight during first 2 months and ≥ 6.4% in the six months of treatment indicates successful treatment outcome.

A study by Phan et al 2016 showed a significant change in weight of tuberculosis patients throughout the treatment. It also pointed a linear pattern of growth in those who had showed weight gain.[18] In the present study, pattern of growth remained similar during the treatment both in first 2 and last 4 months. A South Indian study indicates association between weight gain and DOTS.[11] There was an overall weight gain in patients on DOTS which showed its effectiveness. Our findings are in consonance with the aforesaid study. Body weight loss or minimal gain (< 5%) in initial 2 months of treatment was concluded as a predictor of unsuccessful outcome in a Vietnamese study.[19] The present study also supports the finding. However, unlike our study, this study couldn't find any association between end treatment weight gain and treatment outcome. This might be due to difference in characteristics of study population. A longitudinal study by Bornabe-otiz concluded weight gain in first month as a significant independent factor for treatment outcome.[12] This study indicates that changes in weight over the time are different while comparing poor outcome and good outcome tuberculosis patients. This longitudinal study showed that the patients gained an average 3.3 kg after 5 months of treatment. Our study also found on an average 4 Kg gain after 6 months of treatment. Study from India also confirmed the similar weight gain.[11] This implies DOTS, the sure cure of TB is effective enough in recovering the chronic illness and decreasing the bacterial load. In a similar study in Peru by Krapp et al, unsuccessful outcome was found to be associated with poor weight gain.[13] In this study, 5% of basal weight was considered as cutoff. Similar finding was witnessed in another study by Khan etal, taking the similar cutoff.[20] Krapp et al, couldn't find any association between outcome and initial body weight gain in end of first and 2nd month taking 5% as cutoff. Further in ROC analysis they found that body weight gain at the end of first, second month and end of treatment were useful in predicting treatment outcome. Cutoffs of % body weight gain in predicting outcome (successful/unsuccessful) were found to be 4.5% and 7% at the end of second month and end of treatment respectively.[13] While cutoff at end of six month from our study corroborates with their finding, cutoff of % weight gain during first two months are varied in both the studies. This might be attributed to inclusion of retreatment cases in

our study population, who had already taken treatment and remained unsuccessful or lost to follow up.

There are a few strengths in this study, firstly we prospectively followed up the patients from the initiation of DOTS throughout the treatment; secondly an attempt was made first time in India to find out any cutoff for body weight gain; third, instead of absolute body weight gain, % body weight gain was evaluated assuming varied range of basal body weight. Our study has few limitations, weight gain of all type of tuberculosis cases (pulmonary/extra pulmonary or new/retreatment) are evaluated together assuming response of body weight to DOTS to be similar; second, differential drugs compliance, diet intake and gender could be considered while evaluating the cut off.

CONCLUSION

Based on finding of our study it can be concluded that percentage of body weight gain can be used as an predictor of treatment outcome and patients with poor body weight gain can be identified and followed up meticulously during DOTS. Personalized diet counselling is essential during directly observed treatment short course strategy. Further operational research can be carried out in order to implement this strategy in National Programme.

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