

# Comparison of Directly Observed Treatment Short Course (DOTS) with Self-Administered Therapy in Pulmonary Tuberculosis in Udupi District of Southern India

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## ABSTRACT

**Background:** Directly observed treatment short course (DOTS) and self-administered therapy (SAT) are the treatment options available for tuberculosis (TB). Studies conducted worldwide have shown difference in treatment outcome with these two treatment modalities.

**Aim:** The study was undertaken to compare treatment outcome of DOTS and SAT in patients of pulmonary TB taking SAT from a tertiary care hospital and DOTS from the DOTS centre of a government hospital.

**Materials and Methods:** It was a retrospective comparative study. The case record files of patients with pulmonary TB diagnosed from March 2011 to February 2012 were analysed as per the proforma. The sample size of patients was 150 (75 each from DOTS and SAT).

**Results:** The treatment outcome in DOTS group was cured 70.7%, treatment completed 1.3%, failure 5.3%, deaths 10.7%, defaulters 8% and transferred out 4% whereas in SAT group, cure was seen in 68% and 4% completed the treatment, 1.3% had treatment failure, and 26.7% were lost to follow up which included deaths, defaulters and those patients who switched over to other hospitals. The treatment success rate was similar (72%) in both groups. There was no statistically significant difference observed in the average weight gain at the end of treatment between the two groups. A total of 11 adverse drug reactions (4 DOTS, 7 SAT) were recorded in the study.

**Conclusion:** The study shows no statistically significant difference between success rate in patients taking DOTS and SAT.

**Keywords:** Cure, Defaulters, Treatment completed, Treatment failure, Treatment success, Tuberculosis

## INTRODUCTION

Tuberculosis (TB) is a major public health problem and one of the top killer diseases. Globally, there were 8.7 million estimated incident cases of TB and 1.42 million deaths due to TB in 2011 [1]. India is the highest TB burden country in the world in terms of absolute number of incident cases that occur each year. The revised estimated prevalence and incidence rate of all forms of TB was 256 and 185 cases per 100,000 populations respectively in India in July 2011 [2].

An important aspect of treatment of TB is patient adherence because failure to complete treatment can result in relapse and drug resistance ultimately leading to death. Among the strategies to improve patient adherence, the most important one is directly observed treatment short course (DOTS). Its advantage is that patient can be closely monitored and promotes adherence. It also reduces the prevalence of MDR, reduces the cost per case of TB treated and improves the rate of treatment completion. However, an analysis of series of 11 randomised controlled trials showed no difference between the outcome of DOTS and self-administered therapy (SAT) [3]. Studies have further revealed that the benefits associated with programmes implementing DOT is because of other associated inputs rather than direct observation specifically [4]. In contrast, studies from India have shown that DOTS has higher cure rates compared to SAT [5-7]. With this background, the present study was carried to compare the treatment outcome of the two modalities (DOTS and SAT).

## MATERIALS AND METHODS

The study was carried out after obtaining clearance from the Institutional Ethics Committee, Kasturba Hospital, Manipal, India (letter no. IEC 278/2011). Permission to access patient records was obtained from the Medical Superintendent, Kasturba Hospital,

Manipal as well as from the Joint Director, State Tuberculosis Centre, Bangalore.

It was a retrospective comparative study with a sample size of 150 patients (75 patients from DOTS and SAT). The consecutive case record files of patients with Pulmonary TB, diagnosed between 01 March 2010 and 28 February 2011 were analysed. The record files of 75 patients taking SAT were taken from medical records department of Kasturba hospital, Manipal. The medical records of 75 patients taking DOTS were accessed from DOTS centre, District Government hospital, Udupi.

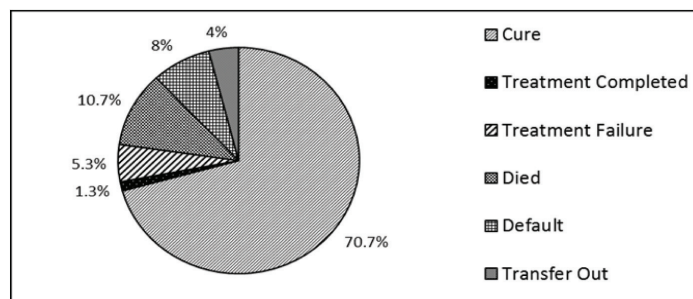
Patients of either sex, aged  $\geq 18$  years and diagnosed with smear positive pulmonary tuberculosis (both newly diagnosed and previously treated patients like defaulters, treatment failure and relapse) were included in the study.

Patients with sputum negative pulmonary TB, MDR TB, extra pulmonary TB or with HIV-AIDS were excluded.

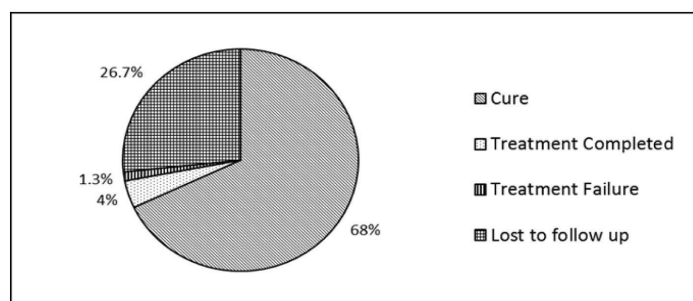
The data collected using the predesigned proforma included - socio-demographic details, clinical features, baseline investigation values, reports of sputum examination, adverse drug reactions and treatment outcome (cure/ treatment completed/ treatment failure/ defaulter/ transferred out/ treatment success/ death) as per WHO guidelines [8]. Cure means sputum smear- or culture-negative in the last month of treatment and on at least one previous occasion. Treatment completed means patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion. Treatment failure means sputum smear or culture is positive at five months or later during treatment. It also includes patients found to harbour a multi-drug resistant (MDR) strain at any point of time during the treatment, whether they are smear-negative or positive. Default means whose treatment was interrupted for two

Baseline characteristics		DOTS (n=75)	SAT (n=75)
Male/female ratio		56/19	55/20
Patient category	New	56 (74.7%)	62 (82.7%)
	Retreatment	19 (25.3%)	13 (17.3%)
Mean age (years)		43.63±13.3	43.75±13.2
Mean haemoglobin (g/dL)		10.73±2.36	11.42±1.59
Patients having associated diabetes mellitus		6	20

[Table/Fig-1]: Baseline characteristics of the study population



[Table/Fig-2]: Treatment outcome in DOTS group (n=75)



[Table/Fig-3]: Treatment outcome in SAT group (n=75)

consecutive months or more. Transfer out has been transferred to another recording and reporting unit and whose treatment outcome is unknown. Treatment success is the sum of cured and completed treatment.

## STATISTICAL ANALYSIS

Data was analysed using SPSS software version 15. Statistical analysis was descriptive. Chi-square test was used to compare the treatment outcome in two groups. Paired t-test was used to compare the change in weight between the two groups. P-value of less than 0.05 was considered statistically significant.

## RESULTS

The medical records of 150 patients (75 each from DOTS and SAT) who were diagnosed to have pulmonary tuberculosis were studied. The baseline characteristics of study population are shown in [Table/Fig-1].

A total of 150 patients were included in the study. In both DOTS and SAT groups, there was a male preponderance and majority of the patients (49%) were in the age group of 41-60 years. The treatment outcome was based on the following parameters: cure/ treatment completed/ treatment failure/ defaulter/ transferred out/ treatment success/ death [8].

**DOTS:** The percentage of patients in DOTS group who completed treatment, had treatment failure, died, defaulted and were transferred out is shown in [Table/Fig-2]. There were six defaulters (four males and two females). Four defaulters were newly diagnosed patients and two were retreatment patients who had interrupted an earlier TB treatment course. Two patients interrupted treatment after one month whereas the remaining four defaulted after taking four months of treatment. The treatment success rate (sum of patients cured and treatment completed divided by total number of patients) in the DOTS group was 72%.

**SAT:** The treatment outcome of patients in SAT group is shown in [Table/Fig-3]. In this group, as there are no home visits and thus no proper recording in the case files regarding patients who did not return for their scheduled visits to the hospital. This subgroup of patients have been considered as lost to follow up and includes deaths, defaulters and those who have switched to other hospitals for treatment. Twenty patients (17 newly diagnosed and three retreatment) in SAT group had interrupted treatment. Out of 17 new patients, 10 defaulted after two months of treatment, three after three months of treatment and remaining four defaulted in the fifth month of treatment. Among the retreatment patients, two of the three took treatment for two months only whereas the third patient completed five months and then stopped treatment. In the SAT group the treatment success rate i.e., sum of patients cured and treatment completed divided by total number of patients was 72%.

**DOTS versus SAT:** There was statistically no significant difference in treatment outcomes between the two groups in terms of cure ( $p>0.05$ ), treatment completed ( $p>0.05$ ) and treatment failure ( $p>0.05$ ). Also, no statistically significant difference ( $p>0.05$ ) in the total number of defaulters, deaths and transferred out cases between the two groups was observed. The treatment success rate (sum of patients cured and treatment completed divided by total number of patients) was same in both the groups i.e., 72%.

Average weight gain at the end of treatment was 4.8 kg in DOTS group and 5.1 kg in SAT group. There was no statistically significant difference ( $p>0.05$ ) in the weight gain between the two groups.

**Adverse Drug Reactions (ADRs):** A total of 11 ADRs were seen in both groups. Of these, four ADRs occurred in the DOTS group. Two patients had rash; one had pruritus and one fever. A total of seven ADRs were recorded in SAT group. Three cases of ATT induced hepatitis, one case each of isoniazid and ethambutol induced rash and two cases of pyrazinamide induced hyperuricemia were observed.

## DISCUSSION

There have been controversies regarding the effectiveness of DOTS and SAT and many feel that patients should be given a chance of SAT before being compulsorily subjected to directly observed therapy. In our study we found that the treatment success rate was equal in both the groups i.e. 72%. Earlier studies [4,9] have shown that the cure rates are similar in DOT and SAT. In contrary, few studies conducted in India showed significant differences in cure rates of patients taking DOTS and SAT. In a study [6] conducted by Verma et al., the cure rate was 91.3% among DOTS group while it was only 34.0% among SAT group. Similarly in another study [5], the cure rate in DOTS group was 91% whereas among SAT group it was 53%. Tandon et al., also found inferior cure rates in SAT (54%) compared to those obtained in DOTS (85%) [7]. The difference in the results of these studies from our study could be primarily because of two reasons. First, the socioeconomic and educational background of the two groups in our study is different. Patients taking DOTS from the government hospital were of poor socioeconomic background whereas those taking SAT from the tertiary care hospital were largely from high-literacy geographical areas of Karnataka and Kerala. Therefore, the SAT group observed higher treatment compliance in present study compared to the former studies, thus resulting in higher cure rates. Second, the small sample size may be responsible for similar cure rates between DOTS and SAT group.

The weight of the patients taken at different time points during treatment is an important component to assess the progress of patient. Numerous studies have showed that patient's body weight is associated with treatment outcome [10-12]. However, some authors put forth that weight gain during antitubercular therapy appeared to be an unreliable indicator of overall treatment response [13]. In our study, in the DOTS group the average weight gain of

patients at the end of treatment was 4.8 kg while that in SAT group it was 5.1kg. In a study [14] conducted at a TB unit in Tamil Nadu, average gain in weight among patients who took DOTS was 3.22kg which is less than that of our study results. There was no statistically significant difference in the mean weight gain at the end of treatment completion between the two groups reflecting that DOTS has no added advantage over SAT in terms of weight gain of the patients.

Like any other drugs, anti-tubercular drugs are not free from adverse reactions. A total of 11 ADRs (four in DOTS and seven in SAT) were seen among patients. All the four reactions in patients receiving DOTS were caused by isoniazid. Isoniazid was stopped in all the cases and the remaining drugs were continued. In SAT, in patients who developed rash, the suspected drugs were stopped. In one patient with hepatitis, rifampicin as well as pyrazinamide was stopped and in the remaining three patients of hepatitis, only pyrazinamide was stopped. In cases of pyrazinamide induced hyperuricemia, the drug was continued and no remedial therapy was given. There was no case of antitubercular therapy induced symptoms of peripheral neuropathy i.e., tingling and burning sensation in hands and feet which is reported to be one of the most common adverse effect in a study conducted in Nepal [15]. This could be because of prophylactic pyridoxine was prescribed to all patients who took SAT and lack of proper ADR recording in DOTS. A higher number of ADRs seen in patients who took SAT compared to DOTS could be because SAT was provided in a tertiary care hospital with better laboratory facilities. In such a setting, health care providers are more vigilant and promptly detect as well as treat ADRs.

It is clear that whether a patient takes treatment with or without supervision, the outcome does not vary as long as he completes the full course of treatment. Failure to adhere to treatment can lead to fatal outcomes like multidrug/ extensive drug resistant TB ultimately resulting in death of patient. Implementation of DOTS is the one of the ways to improve adherence to treatment of TB, especially in a developing country like India. The limitations associated with DOTS are high cost and stigmatization. SAT being a relatively low cost alternative is a better option especially in high TB burden underdeveloped and developing nations [16]. Educating the patients, providing free medications and other incentives to patients and allowing the patient to choose between DOTS and SAT are some of the steps that can enhance patient compliance. Regular checking of empty medicine blister packs, monitoring urinary or blood levels of drugs can further ensure patient compliance.

The present study was retrospective, hence complete information regarding certain aspects of treatment, its outcome and ADRs could not be collected because of missing entries in the case record files. This was a major limitation of our study. The sample size of the study was small and patients suffering from MDR-TB and TB associated with HIV infection were not included. Therefore, treatment outcomes obtained in this study should be cautiously extrapolated to the general population. In addition, patients taking DOTS and SAT in our study were from different socioeconomic and educational background, which could have interfered with the

treatment compliance and thereby final results. Further prospective studies with larger sample size should be carried out to overcome the above shortcomings.

## CONCLUSION

The present study puts forth that there was no significant difference between treatment outcome in patients taking DOTS and SAT. However, it is difficult to comment which of the two is better because each has its advantages and limitations. Hence, it becomes imperative to carry further studies and frame the best possible treatment modality for achieving a "tuberculosis free" world.

**Declaration of Conflicting Interests** - 'The Author(s) declare(s) that there is no conflict of interest'.

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