



COMPARISON OF TREATMENT OUTCOME OF SELF ADMINISTERED ANTI TUBERCULAR THERAPY WITH DIRECT OBSERVATIONAL THERAPY SHORT COURSE IN FEMALE GENITAL TUBERCULOSIS

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ABSTRACT

Female genital tuberculosis is responsible for damage of genital organ & a major cause of infertility and menstrual irregularities in developing countries like India. The present study was aimed to evaluate the comparison of treatment outcome of anti tubercular drugs given in the form of Self Administered Therapy (SAT) & Direct Observational Therapy (DOTS). Total 386 patients (223 for SAT group & 163 for DOTS group) were recruited from the OPD department of Obstetrics and Gynecology, KGMU, Lucknow, diagnosed FGTB. In 6 month treatment 130 (81.2%) patients cured in DOTS group, whereas only 81 (37.9%) cured in SAT group. P-value found 0.01 statistically significant for the DOTS group. A total 14 ADRs were found 3 (1%) SAT & 11 (7%) DOTS group patient respectively. Results showed that DOTS therapy better than the SAT & it helpful for the deprived socioeconomic patients.

KEYWORDS: *DOTS, SAT, FGTB, ADRs.*



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INTRODUCTION

India is the country with the highest burden of tuberculosis (TB) with World Health Organization (WHO) statistics shows 9 million cases of TB, 2.1 million cases are in India¹. Inhalation is the most susceptible pathway of *Mycobacterium tuberculosis* infection, pulmonary tuberculosis being the predominant one. TB affects sites other than pulmonary site known as extra-pulmonary TB (EPTB) which is rarely smear-positive. The percentage of patients with EPTB at tertiary care centers in India was between 30% and 53%². It is reported that the incidence varies and can be as low as 0.69% in developed countries and as high as 19% in India³. Female genital tuberculosis is a form of EPTB affecting the genital organs, with fallopian tubes being affected most commonly (90%), followed by the endometrium (50%) and the ovaries (10-30%)^{4, 15}. The definitive diagnosis in female genital TB is difficult. *M. Tb* being the silent invader of genital tract to create the diagnostic dilemmas because of varied clinical presentations, diverse results on imaging and laparoscopy, limitations of histopathologic, serologic, bacteriologic and culture methods⁵. A correct diagnosis is an important and indispensable part of proper and timely treatment. Physician tends to adopt therapeutic test for elimination of any type of TB by prompt execution of anti tubercular therapy (ATT) i.e., conventional Self Administered Therapy (SAT) or Directly Observed Therapy (DOTS) for the requisite period of time. WHO recommends the tuberculosis control strategy, which is the Directly Observed treatment short course. As per the DOTS strategy, a full course of an anti TB drug, sufficient to cure patient cost \$40, making it the most cost effective health interventions⁶. Effective cure of TB requires a patient taking medication without interruption following a strict schedule for at least 6 months, which is difficult for most patients to maintain. Directly observed treatment (DOT), whereby a trained person observes patients taking their medications, is widely used to improve adherence to treatment⁷. A prescription error or poor compliance can delay the response to treatment, leading to failure and thereby resulting in continuing morbidity, despite the fact that good quality drugs are available. ATT includes five drugs that are most commonly used today to treat tuberculosis, Isoniazid (INH, Laniazid,

Nydrazid); Rifampin (Rifadin, Rimactane); Pyrazinamide (Tebrazid); Streptomycin; and Ethambutol (Myambutol). The first three drugs may be given in a capsule to minimize the number of pills in the dosage. As of 1998, many patients have been given INH and Rifampin together for six months, with Pyrazinamide prescribed only for the first two months. Hospitalization is rarely necessary because most patients are no longer infectious after about two weeks of combination treatment. Follow-up involves monitoring of side effects While under RNTCP, DOTS is a major plank in the WHO Global Plan to Stop TB.

MATERIALS AND METHODS

A total of 386 patients were recruited from Gynae OPD, Department of Obstetrics & Gynecology, King George's Medical College Lucknow. An informed consent was taken from the patient. Relevant history, clinical examination & investigations were recorded. New patients, who has never had treatment for TB, or has been an anti-TB treatment for less than four weeks comes under category I. A patient, who has been completed treatment for any form of TB in the past (or) after previous treatment failure, but who reports back to the positive for tuberculosis comes under category II, given by RNTCP. (Human ethical approval has been attached)

Clinical & Biochemical investigation

The diagnosis of genital tuberculosis was done based on different tests as Montoux test, chest skiagram, erythrocyte sedimentation rate (ESR), histopathological examination (HPE) of pre menstrual endometrial tissue, PCR of *Mycobacterium tuberculosis* DNA from menstrual blood collected on the first day, immunological test of blood, tubercle bacilli by AFB staining culture of menstrual blood or endometrial curetting, and hysterosalpigography (HSG) examinations during day 7-9 of menstrual cycle to see the patency or blockage of fallopian tube. Diagnostic Laparoscopy (DL) and Hysteroscopy were done to see the presence of tubercles & tubercular lesions and can provide adequate histological and bacteriological evidence (Table-1).

Table 1
Lists the % of positive as per the above mentioned tests (n=386)

S. No.	Investigation Done	No. of Patients	Percentage (%)
1	TB PCR (in Menstrual Blood) Detected	245	63.5
2	IgM TB Positive	59	15.3
3	PPD or Montoux Positive	70	18.1
4	AFB (in Menstrual Blood)	70	18.1
5	DL and Hysteroscopy Findings suggestive of tubercular lesion	108	28.0

Drug Regimen

All the available diagnostic techniques were combined judiciously and correlated with the clinical profile prior to initiating the anti tuberculosis treatment. Treatment was initiated after confirmation of FG TB. The patient has been

counselled on the benefits for the same. Anti tubercular therapy either as Self administered therapy (SAT) or as Direct observational therapy (DOTS) were administered on the bases of socioeconomically condition & willing to take type of therapy. Confirmed cases of FG TB were

separated into two groups on the bases of treatment regimen. One group fell into the SAT arm (n=223) of treatment & the other arm were given DOTS (163) and the treatment efficiency was subsequently determined. All the details of the patients were recorded, DOTS were provided to the patients from the DOTS center near their residence. Treatment given initially six months then before completing the therapy, same clinical test was repeated on which basis treatment was given. If the clinical test was negative drug stopped after completing the six months and patient kept on Follow-up. The performed test was positive for the tuberculosis the same drug regimen was continued for the next three months and patient counselled to complete nine months course of the treatment without one day gap for the complete cure of the disease. The patients were followed up every month to check for complications or side effects produced by the drug by history clinical examination and by performing the liver function test (LFT). One month before the completion of the nine month course, the same diagnostic tests were repeated again to confirm the

efficiency of treatment, if test result was negative stopped the drug after completing nine months course and next one year follow up of patient is conducted and if the clinical test result was positive again the patient was counselled for MDR TB treatment for further evaluation.

RESULTS

A total of 386 patients were included in the study, in which majority of the patients fell in the age group of 26-30 years (50%). The categorical differentiation of patients as per as their age group & on the basis of symptoms and complaint listed in Table 2 & Table 3. Baseline characteristics of patients described in Table-3 shows maximum no. of patients presented with primary infertility (68%). On various investigations 63.5% patients had TB-PCR positive but only 28% patients showed tubercular lesion on diagnostic laparoscopy & hysteroscopy findings (Table-1).

Table 2
Number of Patients based on age Group (n=386)

S. No.	Age Group (Years)	No. of Patients	Percentage (%)
1	<25	85	22.0
2	26-30	193	50.0
3	31-35	68	17.6
4	>35	40	10.4

Table 3
Number of patients on the basis of Symptoms and Complain (n=386)

S. No.	Symptoms/Complain	No. of Cases	Percentage (%)
1	Primary	263	68.1
2	Infertility Secondary	51	13.2
3	Primary	6	1.6
4	Amenorrhea Secondary	28	7.3
5	Pain in Lower Abdomen	24	6.2
6	Recurrent Miscarriage	11	2.8
7	Infertility with Pain in Lower Abdomen	3	0.8

Out of 163 patients of DOTS group 160 patients took DOTS category I, out of which 130 (81.2%) patients cured within 6 months while 30 patients continued for 9 months. 3 patients kept on category II. Out of 223 patient

of SAT group 214 patients took SAT category I, out of which 81(37.9%) patients cured within 6 months while 133 patients continued for 9 months. 9 patients kept on category II (Table-4).

Table 4
Distribution of total cases according to duration and Category of Drug (n=386)

Drug Category		No. of patients taken drugs	
		6 Months	9 Months
SAT (n=223)	Category I (n=214)	81 (37.9%)	133 (62.1%)
	Category II (n=9)	9 (100.0%)	0
DOTS (n=163)	Category I (n=160)	130 (81.2%)	30 (18.8%)
	Category II (n=3)	3 (100.0%)	0

Table 5
Response of treatment in 6 month course

Duration(6 month) /Drug category	DOTS(n=160)	SAT(n=214)	RR (95%CI), p-val
Category I	130 (81.2%)	81 (37.9%)	0.51 (0.35-0.74), 0.
Category II	3 (100.0%)	9 (100.0%)	

RR=Relative risk, CI=Confidence interval, *Significant,

The percentage of cure of Category I patients was higher in DOTS compared to SAT and this was 49% significantly lower in SAT than DOTS (RR=0.51, 95%CI=0.35-0.74, p=0.01) at 6 months.

Table 6
Total Cured Patients & conceived in 6 month

Duration(6 month) /Drug category	DOTS(n=160)	SAT(n=214)	RR (95%CI), p-va
Patient cured	130 (81.2%)	81 (37.9%)	1.71 (0.99-2.80), 0
Conceived	3 (1.9%)	6 (2.8%)	

RR=Relative risk, CI=Confidence interval

The percentage of patients cured as checked by different tests (AFB Smear, TB-PCR, PPD,) & cured rate higher among DOTS patients than SAT. However, the conceiving was 1.71 times higher among SAT patients than DOTS (RR=1.71, 95%CI=0.99-2.80, p=0.09 and this was statistically not significant (p>0.05).

DOTS

Of total 163 patients in DOTS group, 150 (92.2%) patients completed the treatment, 13 patients drop out during the study. In 6 months regimen of DOTS, 130 (81.2%) patients cured and 3 (1.9%) patients conceived after completion of treatment (table-6). The efficacy & cure rate of patients in this regimen strategy was (81.2%). There were 4(3%) defaulters, who had an earlier TB treatment course. 1 patient discontinued treatment after one month, whereas the remaining 3 discontinued after 2 months. Two (1%) patients were diagnosed as into MDR-TB, even after completion of 9 months full course (figure-1).

SAT

Of total 223 patients in SAT group, 210 (94.1%) patients completed the treatment & 13 patients drop out during the study. In 6 months regimen of SAT, 81 (37.9%)

patients cured and 6 (2.8%) patients conceived after completion of treatment (table-6). The efficacy & cure rate of patients in this regimen strategy was (37.9%). There were 9 (4%) defaulters found in this treatment group and one of the patient transferred into MDR-TB (figure-2).

DOTS versus SAT

There was a statically significant difference found in treatment outcome in the form of time duration of therapy (6 months & 9 months) in DOTS group i.e. (p=0.0001*), (Table-5). In 6 months Cure rate was 81.2% in DOTS group as compared to SAT group i.e. 37.9%. In DOTS group fewer of patients went for 9 month treatment however, in the SAT group further patient went for 9 months treatment. The percentage(%) of patients cure rate in 6 months who were taking DOTS is high just because in this regimen patient took medicine daily from the DOTS center , so the regular follow up of patient was much easier as compared to SAT group, in which patient took medicine at home & only comes once in a month for follow up. The total treatment outcome in DOTS & SAT group given in pictorially form, depicted as the (%) of patients, who were either cured/defaulters/conceived after treatment/drop out/changed to MDR (Fig.1 & Fig. 2).

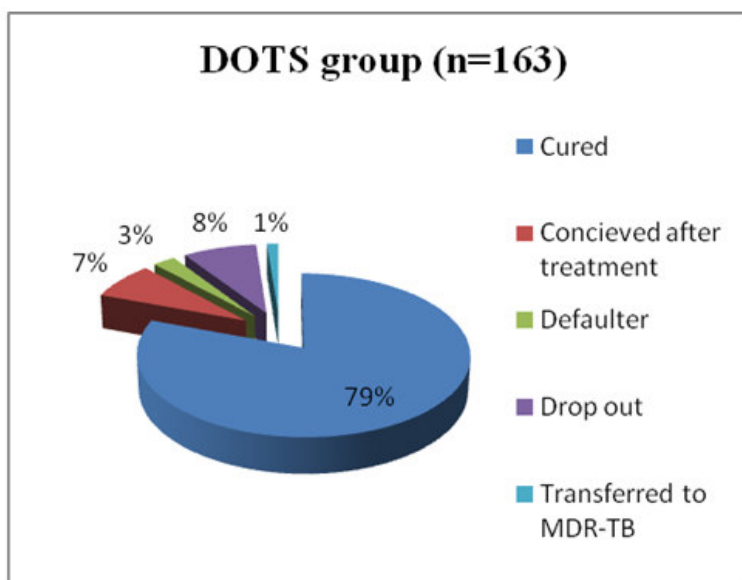


Figure 1

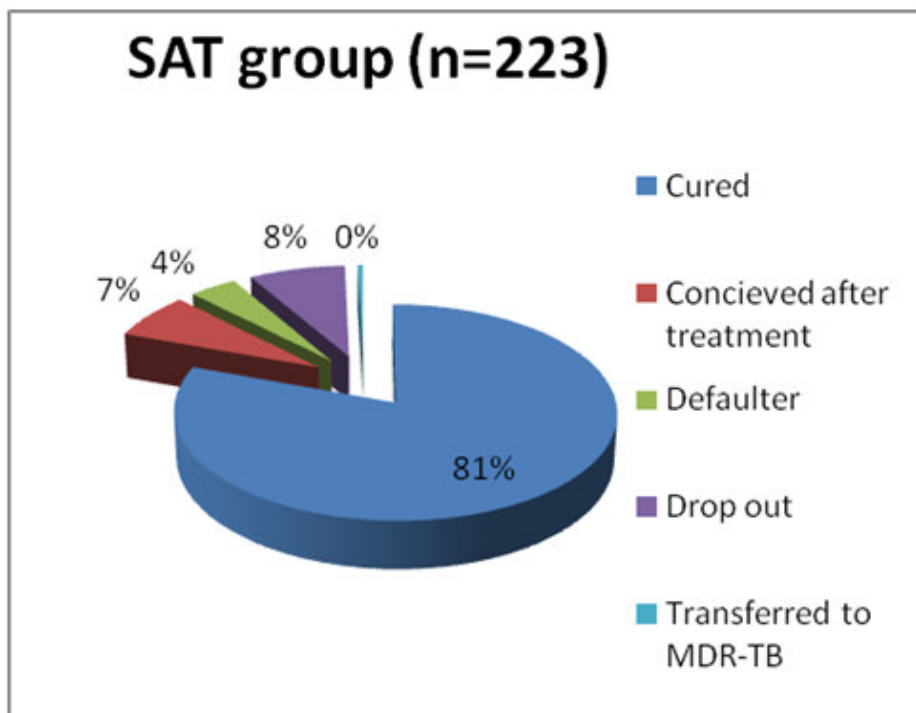


Figure 2

Adverse Drug Reaction (ADR)

A total of 14 patients had ADRs in both groups. Of these, 11 (78.5%) patients ADRs were from DOTS group. In which 3 (27%) patients had skin-rashes; 5 (46%) complained of vomiting and 3 (27%) developed severe fever. Three patients (21%) in SAT group developed ADRs. 1 (33%) patient of SAT suffered from deranged LFT & 1 (33%) with vomiting & fever. It was experienced

that timely detection and temporary withdrawal of the offending agent can completely cure anti-tuberculosis drugs (DOTS) induced side effects. For this, vigilant patient monitoring by hematological and biochemical means during treatment and patient counselling regarding side effects of the anti-tubercular medications are necessary (Fig.3 & Fig 4).

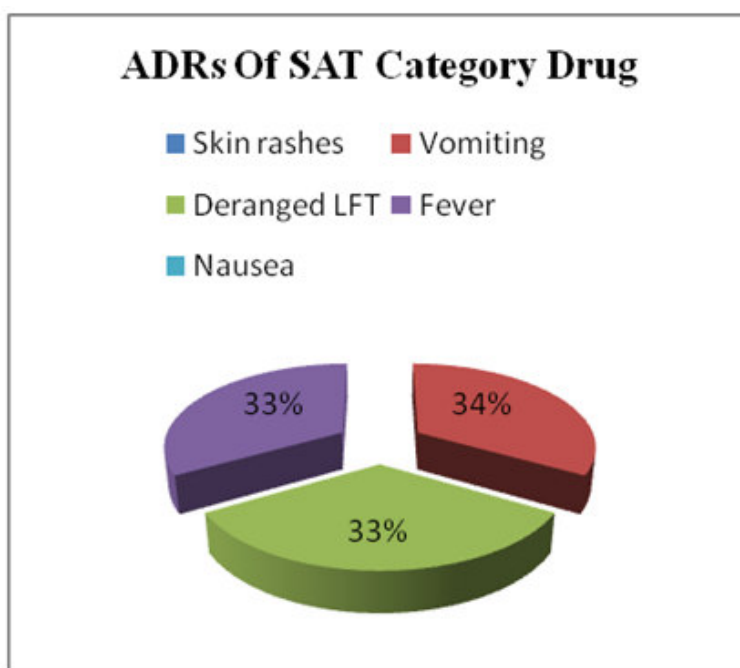


Figure 3

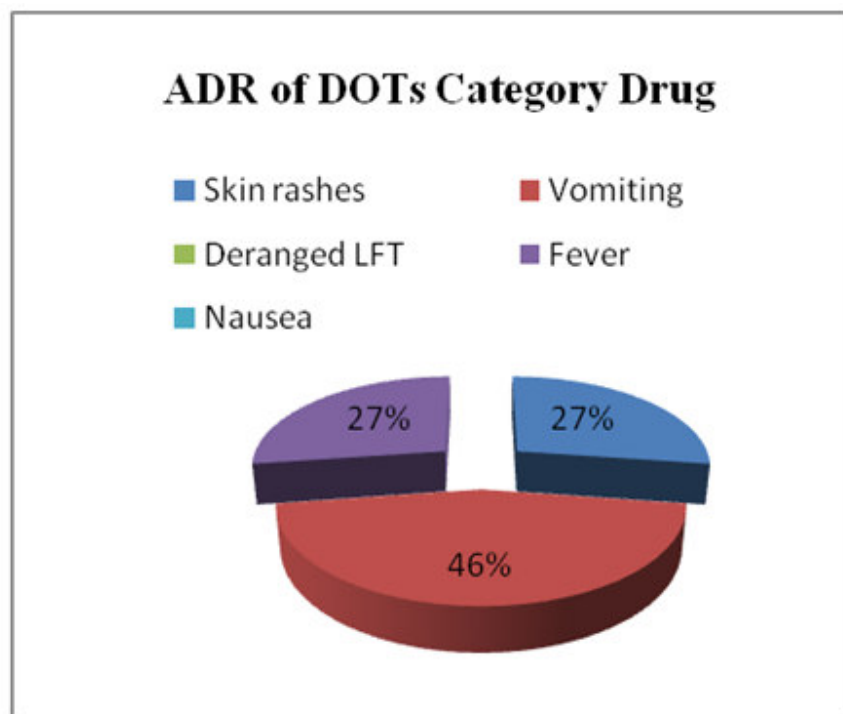


Figure 4

DISCUSSION

There have been controversies regarding the effectiveness of DOTS & SAT. In present study significant difference had seen in treatment success rate of 6 months, i.e. 81.2% in DOTS group and 37.9% in SAT group. The study conducted by Murali et.al, Verma et.al. & Tondon et.al, showed high rate of difference in the cure rate of both therapies^{11, 12, 13}. This is because of socioeconomic & demographic difference in the groups. The above study supports the present study. An earlier study conducted by Barbara et.al using meta-analysis suggested that SAT & DOTS were statically equivalent with respect to microbiologic failure, relapse & ADR⁹. Like any other drugs, antitubercular drugs also have a hepatotoxicity adverse reaction. A total 14 ADRs (11 in DOTS & 4 in SAT) were seen, who developed complaints as skin rashes, vomiting, deranged LFT, the suspected drug was stopped. Another study conducted by Amrita et.al. total no. of ADRs less in DOTS group as compared to SAT group and cure rate was 72% in both groups¹⁰. The overall study shows, that whether a patient taken DOTS with the supervision of hospital & SAT without any supervision, there were no difference in cure rate. In

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CONCLUSION

DOTS failure to regular follow up the patients leads to more towards ADRs & can lead to fatal outcomes like multidrug resistance i.e., MDR.

The present study puts forth that there were significant difference between treatment outcome in patients taking DOTS and SAT in female genital tuberculosis. It is thus concluded that DOTS provided by the Government is better with SAT in treating genital tuberculosis and DOTS can be recommended because it is highly feasible for the economically downtrodden patients. Eradication of female genital tuberculosis can be achieved by creating awareness to the general public about the effectiveness and availability of government provided medicine for TB (DOTS).

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