

Original article:

Long term outcome of DOTS treatment under RNTCP; A 5-years follow up study

¹Dr. Ashok Kumar Mehrotra * , ²Dr. Yugal Tak, ³ Dr. S.P. Agnihotri

¹MD (Resp. Med. & TB), Associate Professor

²MD (Resp. Med. & TB) Medical Officer(RNTCP), Institute of Respiratory Diseases, SMS Medical College, Jaipur

³MD (Resp. Med. & TB) Professor& Head, Institute of Respiratory Diseases, SMS Medical College, Jaipur

Corresponding author*

Abstract

Background: Revised National Tuberculosis program (RNTCP) adopted Direct Observed Treatment –Short Course (DOTS) strategy, intermittent regimen, for the tuberculosis control program in India. RNTCP categorized tuberculosis patients in three categories (Cat-I,Cat-II and Cat-III) and formulated standardized regimen for each category. RNTCP achieved Global targets in 2007 (>70% detection of new sputum smear positive cases and 85% cure rate).For the program monitoring, periodic assessmentof the outcome of program activities is essential. The outcome studies of DOTS treatment have been done by various workers in different clinical settings, which yielded heterogeneous results. The present study was done to evaluate the5 yearsoutcome of DOTS therapy inRNTCP declared successfully completed treatment and cured casesusing relapse, death, unsuccessful outcome and sequelae as parameters of outcome.

Method: This was a retrospective observational cohort study approved by the hospital ethics committee. The study was done on the patients registered under RNTCP at Jaipur urban district, who had been were declared cured or completed treatment between 1 to5 years under DOTS. The data were collected on a self-designedpro forma,with the specially trained area health worker.The data were analysed using Microsoft Office Excel-7.

Conclusion: We observed death in 19.8%, unsuccessful outcome in 10% and relapse in 7.8%.More relapses were observed in Cat-I patient, maximum in the first 12 months, more so in first six months following successful completion of treatment.The sequelae could not be assessed due to operational constraints.

Key words : Directly Supervised Treatment- Short Course Chemotherapy (DOTS), Revised National Tuberculosis Control Program (RNTCP), Category, Long term Follow-up, Relapse, Death, unsuccessful outcome

Introduction

Tuberculosis remains a major public health problem in India and accounts for 1/5th of the global incidence of tuberculosis. ⁽¹⁾RNTCP adopted WHO recommended, DOTS strategy, intermittent regimen, for the Tuberculosis Control Programs for India. DOTS treatment included Cat-I to Cat-III regimens for the treatment of new sputum positive/sputum negative and extra-pulmonary tuberculosis disease. Globally, India's DOTS program is now second only to China's in size. ⁽²⁾DOTS achieved Global targets in case

finding (>70% detection of new sputum positive cases) and cure rate (85%) in 2007.

From the inception of the program, continuous efforts arebeing made to incorporate knowledge, research and experience to improve the outcome of the program.The studies done on the outcome of DOTS treatment were in various clinical settings, using various parameters like cure rate, default, treatment failure rate and death, which yielded heterogeneous results. Only few long term outcome studies on DOTS treatment are available in the literature. ⁽³⁻⁷⁾Present study was planned to study

the outcome of DOTS treatment under RNTCP, in patients declared successfully completed treatment including cure at least 1-5 years before inclusion in the study.

Objective

To evaluate the long term (5years) outcome of the treatment completed and cured cases of DOTS regimens under RNTCP using relapse, death, unsuccessful outcome and sequelae as parameters of outcome.

Methodology

This was a retrospective observational cohort study approved by the hospital ethics committee. The study was done on the patients registered under RNTCP at Jaipur urban district.

The inclusion criteria included all patients registered at DOTS clinic in the last 5 years at the Institute of Respiratory Diseases, Jaipur, Rajasthan who had been declared cured or treatment completed at least 1 year prior to inclusion in the study.

The exclusion criteria included;

1. Patients, who did not retrieve for treatment.
2. Patients who had not completed 1 year after being declared cured or completed treatment at the time of inclusion under the study.
3. The patients expired before the completing optimum treatment
4. The patients could not be traced due to incomplete or change of address in the records.

The primary input for the study was the RNTCP reference register from where the patient's details were retrieved.

The present health status was collected by personal visit by health staff at the home or work place of the patient. The patients were interviewed and the information gathered about their health status. In

case of those patients reported died, the information was obtained from the family members. The information was entered into a self-designed proforma,(Annexure-1) The data was later analysed and processed using Microsoft Office 10 Excelprogram.

All symptomatic patients were offered re-investigations which included two sputum examinations, one spot and one overnight for acid fast bacilli (AFB), , Grams stain, pyogenic culture & sensitivity, fungal elements, chest x-ray, complete blood count, random blood sugar, blood urea, serum creatinine, HIV and any specific investigation, if required. A repeat sputum examination for AFB was done after 7-10 day course of antibiotics, wherever advised by the consultant.

The following definitions were used to interpret the observations;⁽²⁾

Relapse; A patient declared cured of TB by a physician, but who reports back to the health service and is found to be bacteriologically positive.

Symptomatic; A patient who had any of the complaints, like cough, expectoration, fever, chest pain, haemoptysis, shortness of breath, weight loss, pedal edema or anasarca in any combination.

Treatment completion; Sputum smear-positive case who has completed treatment, with negative smears at the end of the initial phase, but none at the end of treatment Or: Sputum smear-negative patient who has received a full course of treatment and has not becomes smear-positive during or at the end of treatment Or: Extra-pulmonary patient who has received a full course of treatment and has not become smear-positive during or at the end of treatment.

Cured; A sputum smear positive patient for AFB who had been declared smear negative on two

occasions, one of which was at the completion of the optimum course of treatment.

Sequelae: The after effects of the disease (tuberculosis) like fibro-cavitary disease, bronchiectasis, air way disease, cor-pulmonale and amyloidosis.

Complication; An unanticipated problem aroused with the ongoing tubercular disease like haemoptysis, pneumothorax etc.

Statistical Analysis was done using MS Office Excel 7 software.

Results

A total of 500 cases were included in the study. The age ranged from 5 years to over 65 years with mean age; 39.79 ± 14.6 . 87.8% patients were in the range of 16-55 years of age. (Table-2) 313 (62.6%) patients were male and 187 (37.4%) were female. The male to female ratio observed was 1.67:1. (Table-3) 347/500 (69.4%) were either illiterate or studied up to primary level and rest 153 (30.6%) were educated from middle to post graduate level. The patients were classified into three categories as per RNTCP norm, into Cat-I, which included 167 patients Cat-II; 109 patients (all retreatment sputum positive patients) and Cat-III; 224 patients. 426 (85.2%) patients had pulmonary disease [162 (32.4%) new sputum smear positive, 155 (31%) sputum smear negative and 109 (21.8%) sputum smear positive retreatment patients] and 74 (14.8%) had extra pulmonary disease. (Table- 4) Among the extra pulmonary disease lymphadenitis followed by pleural effusion ranked high, 52.7% and 37.83% respectively. CNS, bone tuberculosis cases were less in numbers.

Out of 500, 99 (19.8%) patients [33 (6.6%) in Cat-I, 46 (9.2%) in Cat-II and 20 (4%) in Cat-III] were reported died between completion of treatment and when first contacted by the health staff. The deaths were almost evenly distributed, annually, over 5-years. More number of deaths were recorded in

Cat-II as compared to CAT-I and III, but the difference did not gain statistical significance ($p=0.75$). (Table-5) 51% deaths occurred in 26-45 years age group patients. The causes of death included, respiratory illness (60%), massive haemoptysis (4%), road traffic accident (RTA), malignancy; 1 (1.02%) each and cause not known in 33 (33%). (Table-6)

In 401 survivors, 66/401 (16.45%) patients were symptomatic and 335/401 (83.54%) were asymptomatic, at the time of first contact. (Table-7) Among the survivors, 30 (7.48%) patients relapsed over 5-years follow up period. [18 in Cat-I, 4 in Cat-II and 8 in Cat-III]. Significantly more relapses occurred in Cat-I ($p=0.001$), in first 12 months ($p=0.001$). (Table-8)

The unfavourable response included, relapse and death combined. The unfavourable outcome was observed in 51/500 (10.2%) in Cat-I, 50/500 (10%) in Cat-II and 28/500 (5.6%) in Cat-III. (Table-8) Apparently all most equal number of unfavourable outcome was observed in Cat-I and II, but unfavourable response turned out to be statistically more significant in Cat-I. ($p=0.019$).

Discussion

In our study 87.8% patients were in 16-45 years group, 62.7% were Male and 37.4% female (M:F ratio; 1.67:1) and 69.4% were illiterate or educated upto primary standard. Others also observed similar patient profile in their study group.^(2,8-10) 83.54% of our patients were asymptomatic when first contacted. Chadha et al. and Dholakia et al. also reported 75% & 82% asymptomatic patients respectively, in their study.^(9,11)

Among our study group 85.2% patients had pulmonary and 14.8% extra pulmonary disease. Others also reported pulmonary disease in 95.16%, 92.6% and 90.78% and extra pulmonary disease in 4.84%, 7.4% and 9.21% respectively.⁽⁸⁻¹⁰⁾ Khatri et

al. observed extra pulmonary sputum smear negative disease in 15% patients in his study.⁽²⁾ Sharma & Mohan et al. has also quoted extra pulmonary tuberculosis in 15-20%.⁽¹²⁾ Our observation was more near to Khatri and Sharma & Mohan.^(2,12) We found our programme performance satisfactory (new sputum positive to negative ratio in our study was [162:155(1.04 :1)]. This was comparable to RNTCP performance status of 1:1⁽²⁾

Relapse

In our study, 7.48 % (30/401) relapses were recorded in all categories, over 5 years study period. This was comparable to Mehra et al., Verma et al., Kant et al., and yatin et al. who also observed relapse in 2.5%, 7.2% and 4.5% respectively in 5 years followup.⁽³⁻⁶⁾ Considering relapses in various categories, 60% (18/30) relapses occurred in Cat-I, 13.33% (4/30) in Cat-II, and 26.22% (8/30) in Cat-III. The relapse was significantly more in Cat-I. (p=0.005). Kant et al., yatin et al., Thomas et al. and Narahari et al. also observed more relapse in Cat-I.^(5,6,13,14) We attribute this mainly to initial drug resistance. Thomas held similar opinion.⁽¹³⁾ Narahari et al. opined that relapse occur due to the quiescent bacterial population, which did not proliferate during the initial treatment.⁽¹⁴⁾ The other causes of relapse include irregular treatment, high bacterial load, cavitory and advanced disease, late conversion⁽¹⁴⁾ and smoking.⁽¹³⁾ Comparing the time of relapse following treatment completion, we observed that, in all categories combined, 23/30 (76.66%) relapses occurred in the first 12 months [16(53.33%) in 0-6 months and 7(23.33%) on 7-12 months], 3/30(10%) in 13-36 months and 4/30(11.2%) after 36 months to the end of the study period. Yatin et al. observed 88.5% relapses in the first year after the completion of treatment.⁽⁶⁾ Thomas et al. observed 12% relapses

in first 12 months and 77% relapses in the first 6 months⁽¹³⁾.

Death

We observed overall higher (19.4%) deaths in our study over 5 years follow up. The deaths were evenly distributed over the study period. The various causes of death reported in our study have been tabulated in table -6. Respiratory related causes and massive haemoptysis contributed to 64% deaths. Analysing the death statistics we observed 6.6% (33) deaths in Cat-I, 9.2% (46) in cat II and 4% (20) in Cat-III. In terms of numbers more deaths occurred in Cat-II but this could not achieve statistical significance (p=0.75). The deaths in our study were much higher as compared to RNTCP (4%), Yatin et al. (6.43%), Jyotiet al. (5.6%), Cao et al. (8.5%), Doulogouet al. (8%).^(3,6,15,16) We postulate that post tuberculosis sequelae contributed to higher deaths in our study. Cao et al. held the opinion that higher mortality rate in retreatment cases was not attributable to relapse of disease, but rather to non-infectious sequelae of tuberculosis.⁽¹³⁾ Khatri et al. and others also observed higher deaths in their Cat-II patients ranging from 8-13% in India.^(2,3-5)

We failed to assess sequelae in our study due to operational issues.

Conclusion

We observed higher (19.8%) deaths in our study over 5 years follow up. The overall relapse observed over 5-years was 7.48%. Maximum relapses occurred in the first 12 months period and the most in the first 6 months following the completion of DOTS treatment. The unsatisfactory results occurred equally in both Cat-I and Cat-II and the difference was statistically insignificant. Larger studies are required to confirm these findings.

Table -1

Classification of Tuberculosis patient and DOTS treatment regimens under RNTCP²

Category	Description	Prescribed Treatment regimens under RNTCP	
CAT -I	i. All new sputum AFB smear positive patients	Intensive phase (IP)	Continuous phase(CP)
	ii. All seriously ill sputum AFB negative patients		
	iii. All seriously ill extra pulmonary tuberculosis patients	2R ₃ H ₃ Z ₃ E ₃ *	4R ₃ H ₃
CAT-II	i. All sputum smear positive relapse	2H ₃ R ₃ Z ₃ E ₃ S ₃ /	5H ₃ R ₃ E ₃
	ii. All sputum positive treatment defaults	1H ₃ R ₃ Z ₃ E ₃	
	iii. All sputum positive failure cases		
CAT- III	All not seriously ill sputum negative pulmonary and extra pulmonary cases	2H ₃ R ₃ Z ₃	4H ₃ R ₃

[(2R₃H₃Z₃E₃) Initial number denotes months and sub script number denotes frequency in days per week.

Table-2

Age wise distribution of Patients

Age-group	Number	Percentage
5-15	4	0.8
16-25	119	23.8
26-35	159	31.8
36-45	84	16.8
46-55	73	14.6
56-65	32	6.4
65+	29	5.8
Total	500	100%

72.2% of patients were in the 16-45 years(361/500)

Table-3
Sex wise distribution

Sex	Cat-I	Cat-II	Cat-III	Total	% of total
Male	101	81	131	313	62.5%
Female	66	28	93	187	37.5%
Total	167	109	224	500	100%

62.5% were male and 37.5% were female (M:F ratio 1.67:1) 167 were in Cat-I(101 male ,66 female),109 in Cat-II(81 male,28 female) and 224 were I Cat-IV(131 male and 93 female)

Table-4
Disease wise and category wise distribution

	Cat-I	Cat-II	Cat-III	Total(Percentage)
Pulmonary	162	109	155	426(85.2%)
Extra pulmonary	5	0	69	74(14.8%)
Total	167	109	224	500(100%)

pulmonary tuberculosis accounted for 85.2% and 14.8% werethe extrapulmonary disease patients

Table- 5
Category wise distribution of death in relation to time after completion of treatment

Category	Total number in each category	Years after completion of treatment				Total deaths (%)
		1 year	2year	3Year	4-5Year	
Cat-I	167	7	6	7	13	33(6.6%)
Cat-II	109	11	9	8	18	46(9.2%)
Cat-III	224	3	6	6	5	20(4%)
Total	500	21	21	21	36	99(100%)

Out of the 500 patient, 99(19.8%) died over 5 years followup. More deaths occurred in Cat-II but the difference was not statistically significant. (p=0.75)

Table-6

Table showing the cause of death (n=99)

S.no.	Cause	Number	Percentage
1	Respiratory ailments	60	60.6%
2	Massive haemoptysis	04	4%
3	Malignancy	01	1%
4	Road Traffic Accident	01	1%
5	Natural and unknown cause	33	33.33%
		99	100%

60% deaths occurred due to Respiratory ailments, specific diagnosis in individual case could not be explored

Table-7

Category wise distribution of symptomatics, asymptomatics among the survivors

Category	Survivors [Total in category (-)Death]	Symptom wise status among remainings	
		Symptomatics	Asymptomatics
Cat-I	167-33=134	25(18.65%)	109(81.34%)
Cat-II	109-46=63	11(17.4%)	52(82.53%)
Cat-III	224-20=204	30(14.7%)	174(85.29%)
Total	500-99=401	66(16.45%)	335(83.54)

83.54% patients were Asymptomatics and 16.45% were symptomatics at the time of first contact by the health staff.

Table-8

Table showing over all out come of DOTS treatment over 5 years

n=500

Category	No. of Patients in each category	Reported Dead	No. of Survivors In each category	Relapse	Unfavorable response
Cat-1	167	33	134	18	51
Cat-II	109	46	63	4	50
Cat-III	224	20	204	8	28
Total	500	99	401	30	129

Out of 500 patients qualified for inclusion, 99(19.8%) were found died at first visit, 16.54 % were symptomatics. Our of symptomatics 30(7.48%) relapsed during 5 years followup, and unfavourable response was observed in 129(32.1%).

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