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Original Research Article

STUDY OF RECURRENCE IN DOTS CURED AND COMPLETED TREATMENT PATIENTS UNDER RNTCP

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ABSTRACT

Background: Recurrences potentially contribute to the spread of new tuberculosis infection in the community. Early identification and treatment of recurrences can effectively break the chain of transmission and reduce the incidence of new infection and disease. The study was done to find out methods for the early detection of recurrence, and the pattern of recurrence, in DOTS (Directly Observed Treatment Short course) cured and completed treatment patients." **Methods:** This was a retrospective observational cohort study, approved by the Hospital Ethic Committee. It was done on the DOTS declared, cured and treatment completed patients, 1-5 years earlier, under Revised National Tuberculosis Control Program (RNTCP) at Jaipur Urban district. **Result:** 16.45% successfully completed DOTS treated patients were found symptomatic. About half of them were diagnosed as recurrence. Significantly more symptomatic and recurrences were observed, in new sputum smear-positive (NSP) patients. Recurrences markedly reduce after the first 12 months of completion of DOTS treatment. **Conclusion:** Monthly follow up of DOTS cured and completed treatment NSP patients for 12 months is suggested. The RNTCP Technical and Operational Guidelines-2016, now advocates a regular follow-up of all cured and successful treatment cases every 6 months, for up to 2 years. Monthly follow-up may be more rewarding than delaying first follow up for 6 months. The RNTCP Guidelines-2016 needs to be reviewed in the light of available evidences.

Keywords: Retreatment, Recurrence, Relapse, follow- up, RNTCP, DOTS

INTRODUCTION

RNTCP convincingly and consistently achieved, the set Global targets in case finding and treatment since 2007, still, the cure rate remained only 59% and the remaining 41% are the left-overs in the community. **(1)** The focus of tuberculosis control program has been on the detection and cures of new sputum positive (NSP) case, whereas 24%-33% of all sputum smear AFB positive cases detected under RNTCP are the retreatment cases **(2, 3)**. Retreatment has remained the grey area in the past and has failed to draw the attention of researchers in the Tuberculosis Control Program; Globally. **(4)** Recurrence is an important cause for the retreatment in tuberculosis besides treatment default and treatment failure. India has

a high (average 10%)rate of recurrence.**(3)** 32% of these recurrences, globally, are caused by multi-drug resistant tuberculosis (MDR-TB)infection. **(5)** We are of the opinion that recurrence is a large source of hidden tuberculosis infection in the community, responsible for the incidence of new infection and disease. We hypothesize that before the DOTS cured and completed treatment patients develop bacteriological recurrence, they should develop disease symptoms. If these symptomatic are timely detected and treated, it can reduce the quantum of tubercular infection in the community and reduce the chances of transmission of new infection and disease. This can be a simple and effective strategy for a quick control of tuberculosis even in the field conditions.

Aims & Objectives

To test our hypothesis that;

- cured and completed treatment patients, develop symptoms before the clinical recurrence occur,
- "active screening for the reappearance of symptoms" by regular follow-up of these cases can be an effective tool for detecting the recurrence,
- To study the pattern of occurrence of recurrence on a long-term basis.

MATERIAL AND METHODS

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, Rajasthan, India on the patients who were declared successfully completed treatment under DOTS at least 1 year before the inclusion in the study.

The primary input for the study, the names, address, treatment details of patients etc. was obtained from the RNTCP reference register. Based on their treatment records, the patients were divided into 2 groups; Group-1 consisted of new pulmonary sputum smear positive (NSP) cases and new extra-pulmonary cases. Group-2 consisted of the retreatment cases. Retreatment Group-II was further divided into two subgroups. Subgroup-2a included smear positive retreatment patients, defaulters and treatment failure cases and Subgroup-2b consisted of retreatment sputum smear-negative pulmonary and extra-pulmonary symptomatic cases, suspected having active disease. The patient data, including his/her registered mobile number, was used to locate the patients. Specially trained, area health staff was deputed to visit these patients, at home or at their workplace, as per their convenience and their health status was collected and recorded on a simple self-devised format and analysed. (Annexure-I) The asymptomatic and the symptomatic were segregated. The patients, who could be traced, but reported dead, their probable cause of death was obtained from the family members. All symptomatic patients were offered investigations which included sputum examination for acid-fast bacilli (AFB), Grams stain, pyogenic culture & sensitivity and fungal elements, chest x-ray, complete blood count, random blood sugar, renal function and liver function test and any other investigation, as required. The disease activity in pediatric age group (5-15 years) and extra-pulmonary patients were clinically assessed by a consultant and included in the study if the disease was considered active. A recurrence was labelled only when a patient was found sputum smear positive for AFB. The further routing of the patients was done as per RNTCP guidelines. A repeat sputum examination for AFB was done

over a 7-10 day course of antibiotics wherever advised by the consultant.

Inclusion criteria: All patients registered at DOTS clinic at the Institute of Respiratory Diseases, Jaipur, Rajasthan, who were declared cured or treatment completed DOTS treatment under RNTCP, within 1-5years at the time of inclusion in the study.

Exclusion criteria: The exclusion criteria included (i) patients not completed at least 1 year after treatment (ii) treatment defaulter (iii) treatment failure (iv) migrated patients (v)Transferred in and transferred out (vi) died before the completion of DOTS therapy, (vii) patients not traceable due to incomplete address.

The following RNTCP definitions were used to interpret the observations;

Cured; A sputum smear positive patient for acid-fast bacilli (AFB) who had been declared smear negative on two occasions, one of which was at the completion of the optimum course of treatment.

Completed Treatment; A 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: an Extra-pulmonary patient who has received a full course of treatment and has not become smear-positive during or at the end of treatment.

Successful treatment completed; included cured and or treatment completed patients.

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

- Symptomatic; A patient, who has complaints of one or any combination of a cough, expectoration, chest pain, haemoptysis for 2 weeks duration or more.
- Asymptomatic; A patient having none of the above respiratory symptoms
- Reinfection; Recurrence with a different strain that has caused the first episode**.(4)**
- Recurrence; Second episode occurring after the cure of the first episode of tuberculosis.**(4)**

Statistical Analysis was done using Microsoft office-7 excel software.

RESULTS

500 DOTS cured and treatment completed patients, who fulfilled the inclusion criteria, were included in the study. The age of the patients ranged from 5 to over 65 years with a mean age of 36.79±14.6. 72.4% of patients were in the range of 16-45years of age. 313 (62.6%) patients were male and the 187 (37.4%) were female (M: F ratio1.6:1.). 69.4% of our patients were either illiterate or studied up to primary level and the rest 30.6% were educated up to middle and above. The distribution of pulmonary and extrapulmonary disease has been tabulated in table-1

Table -1 Disease wise distribution of patients

S.no.	Group-1(n=167)		Group-2(n=333)			
			Group 2a		Group 2b	
	NSP*	EP**	SSP***	EP	SSN****	EP
1	162	5	109	---	155	69

NSP*= New sputum smear positive, EP**= New Serious Extra Pulmonary TB, SSP***= Sputum smear positive, SSN****= Sputum smear negative, EP = Previously treated extrapulmonary

Total 426 (85.2%) patient had the pulmonary disease and 74 (14.8%) had the extrapulmonary disease, including 4 pediatric age group patients.

The distribution of patients, deaths, and symptomatic status has been shown in table- 2.

Table-2 Distribution of Patients, Deaths and Symptomatic status

S.no	Group	Total Number	Died	Total Survivors	Symptom Status	
					Asymptomatic	Symptomatic
1	Group -1	167	33	134	109(81.34%)	25(18.66%)
2	Group-2a	109	46	63	52(82.54%)	11(17.46%)
3	Group-2b	224	20	204	174(85.30%)	30(14.70%)
	Total	500	99 (19.8%)	401 (80.2%)	335 (93.54%)	66 (16.45%)

99(19.8%) deaths were reported in all groups combined at various time intervals after the completion of treatment. In terms of percentage, more percentile death (42.2%) was observed in Group-2a but statistically significant deaths occurred in Group-1. (p=.005, 99% CI 2.58-4.33) Among the survivors, 16.45% had respiratory symptoms (symptomatic). All most equal percentage of symptomatic were observed in all the groups, but statistically significant symptomatic were observed in NSP Group-I patients. (p=.012, 99% CI 2.58-3.36) The pattern of recurrence has been tabulated in table-3.

Table-3 Distribution of Recurrence in Relation to Time after Completion of Treatment

Group	No of survivors	No. of recurrences	Duration of recurrence after completion of treatment in months(M)			
			0-6 M	7-12M	13-36M	37-60M
Group-1	134	18(13.4%)	11(61.1%)	4(22.2%)	2(11.1%)	1(5.5%)
Group-2a	63	4(6.3%)	3(75%)	---	---	1(25%)
Group-2b	204	8(3.9%)	2(25%)	3(37.5%)	1(12.5%)	2(24%)
Total	401	30(7.48%)	16(53.3%)	7(23.33%)	3(10%)	4(13.33%)

Overall 30 (7.8%) recurrences occurred in all groups combined, 53.33% in the initial 6 months (p=0.010, 99% CI 2.58-3.53) out of the total 76.66% in the first 12 months (p=.005, 99% CI 2.58-4.02) after the completion of treatment. These findings were statistically significant. Rest 7 recurrences occurred between 1-5 years.

Among the constituent groups, 13.4% recurrence were observed in NSP Group-1 (p=0.005, 99% CI 2.58- 3.64), 83.33% in 12 months (p=.002, 99% CI 2.58- 4.93) out of which 61.1% in the initial 6 months (p=.010, 99% CI 2.58- 4.32). These findings were highly statistically significant. The recurrence rate reduced proportionately after initial 6th month with the passage of time; 22.22% in 7-12 months, 11.11%

in 13-36 months and 5.5% in 37-60 months. In retreatment, sputum positive Group-2a, 75% recurrences occurred in the first 6 months, none in 7-36 months and 25% between 37-60months, but this finding did not gain statistical significance (p=.111, 99% CI 2.58-2.77). In sputum negative retreatment group-2b patients, 62.5% recurrence occurred in the first 12 months but over the total study duration, recurrences in group 2b did not follow any pattern, as shown in the table-3.

DISCUSSION

72.4% patients in our study, were in the age group of 16-45 years, 62.7% patients were male and 37.4% were female (M; F 1.67:1). 69.4% of patients were either illiterate or educated up to primary standard and 30.6% were educated up to middle and above. Others also observed similar patient profile in their studies. **(6-9)** 83.54% patients in our study were asymptomatic. Our findings were in accordance with Chadha et al. and Dholakia et al. have reported 75% & 82% asymptomatic respectively in their study. **(8, 10)** 85.2% of our patients had pulmonary and 14.8% extra-pulmonary disease. Jyothi et al., Chadha et al. and Chaudhary et al. observed less extra-pulmonary disease in 4.84%, 7.4%, and 9.21% respectively,**(7-9)** while Khatri et al., Sharma &Mohan reported extrapulmonary tuberculosis in 15-20%. **(6,11)** Our observations are more near to Khatri et al. and Sharma & Mohan. **(6, 11)**

Symptomatic: Among the survivors in all groups combined, 16.45% patients had symptoms. Almost equal percentile symptomatic were observed in each group but statistically significant symptomatic were observed in NSP Group-1 (p=.012, 99% CI 2.58-3.36). *Almost half of these symptomatic (45.45%) were detected sputum smear positive recurrences. This was an important observation* in support of our hypothesis. The presence of symptoms in treatment completed and cured cases have not been studied earlier, as the RNTCP had no provisions of follow-up of these cases for any period of time. **(3)** Because of the paucity of the comparable data, this could not be compared with peer groups. Further studies are suggested.

Relapse, Recurrence, Reinfection, and Retreatment

RNTCP defines "Relapse" as a patient, who had been declared cured or treatment completed, earlier by a TB physician, and is now again found sputum smear positive for AFB, when report back to the health facility. RNTCP has not defined recurrence. Others defined "Recurrence", as "the second episode of tuberculosis, after the cure of the first episode". **(12)** Recurrences are known to occur in Tuberculosis. Relapse and recurrence sound same but recurrence may be a true relapse or a reinfection Relapse or Reinfection? The question can be decided by genotyping studies. True relapse can only occur when tuberculosis bacilli persist after treatment despite an apparent cure. **(12)** Relapse occurs with the same genotype and usually preserve the drug sensitivity of the first episode, **(12)** but the sensitivity pattern may not be the preserved due to development of drug resistance. **(13)** The reinfection occurs with a different genotype.**(12)** The clinical implication lies in deciding the drugs for the retreatment regimen. We preferred the term "recurrence" because molecular genotyping was not done in our study. **(2)** The recurrence rate can be taken as an indicator of the efficacy of the tuberculosis control program. **(12)** Recurrences are known to occur in tuberculosis and are the main cause of retreatment, besides treatment failure and default. 24-33% of the total sputum positive cases detected under RNTCP come from the retreatment group. **(2-3)** Azhar et al. have

reported, the combined average rate of default plus failure, as 11.1%±6.7% by culture-based study and 10.0%±7.5% by smear based study. **(3)** The rest of sputum positive retreatment cases diagnosed under RNTCP should logically come from the relapsed cases. The relapse rate is high in India **(3)** and this is an important cause of retreatment. Relapse can occur only in cured and or completed treatment patients. Rusen et al. have observed that completed treatment patients, alone, accounts for 40% of the retreatment cases. **(4)** Das et al. using molecular technique observed 88% recurrences occur due to reactivation and 12% due to reinfection. **(14)** Shen et al. observed 41.8% recurrence occur by different genotype **(15)** suggesting reinfection. It is opinioned that recurrences which occur shortly after the completion of treatment are actually the "relapse. Das et al. and Bandera et al. specified time for recurrence as 3 and 6 months respectively after the end of first treatment. **(16, 17)** In the BMRC trials, most of the recurrences occurred in the first 6 months post-therapy. **(18)** Caminero et al. defined recurrence as a positive culture, at least 12 months, after the last positive culture of the first episode. **(19)** Marie-Laurence is of the opinion that recurrence can occur at any time after treatment of the first episode. **(12)**

Recurrence rate: We observed 7.48% recurrences in all groups combined, against the RNTCP relapse rate of 10%. **(3)** Variable recurrence rates have been reported using sputum smear examination, or sputum culture examination or both ranging from 6.5-12.3% in India **(20-23)** and 0-14% from abroad. **(23)** This has been attributed to the difference in the settings in which the studies were being done.**(3)**

The pattern of recurrence: We observed 76.66% recurrences in all groups combined in our study, in the first 12 months, out of which 53.33% occurred in the initial 6 months after the completion of DOTS treatment. Earlier studies have reported a relapse rate of 68.5% -91% in first 12 months and 50%-77% in initial 6 months. **(16-19, 21-22, 24-25)** Our findings are in accordance with the earlier studies. Out of the total recurrence, NSP Group-1 contributed to the maximum (13.4%) recurrences; 61.1% in the initial 6 months and total 83.3% in the first 12 months after the completion of DOTS treatment. Danial et al. also reported high recurrence in their smear-positive patients cured under DOTS. **(26)** Thomas et al., Narendra Kumar et al., Mitchison et al. and Mallory et al. also held a similar opinion and were of the view that recurrences in Cat-I occur due to high initial drug resistance to one or two primary drugs Isoniazid (H) and Rifampicin (R).**(22,25,27,28)** We further observed that most recurrences occur in the initial 6 months and maximum in the first 12 months and recurrences are markedly reduced after 12 months after completion of treatment (61.1% in initial 6 months to 21.2% in next 7-12 months, 11.1% in13-36 months and 5.5% in 37-60 months). This was another important observation, in the pattern of recurrence. Further studies are recommended.

In the retreatment group, we observed recurrences in 4.9% patients. Cao et al. have reported 5.6% recurrence in their retreatment patients. **(29)** We observed 75% recurrence in sputum positive retreatment Group-2a patients in the initial 6 months, none in 7-36 months and rest one i.e. 25% in 37-60 months. The finding did not gain statistical significance, maybe because of very small number of patients in this group. We attribute recurrence in this Group-2a due to acquired poly-drug resistance, may be due to the addition of single anti-tubercular drug streptomycin, to already failed Cat-1 regimen. Azhar et al. have expressed apprehension about the efficacy of RNTCP Cat-2 regimen.**(3)** Panda et al. reported a threefold rise of polydrug

resistance, in retreatment cases.**(13)** Recurrence in TB occurs either due to reactivation or exogenous reinfection. **(30)** De et al. are of the opinion that in the areas of high TB prevalence, the chances of reinfection from the environment are more. **(30)** A Single late recurrence in this subgroup-2a may be attributed more due to reinfection but endogenous reactivation could not be ruled out, without molecular genotyping studies. Sahadevan et al. are of the opinion that 69% recurrences in India are due to endogenous re-activation. **(31)** Shen et al. observed 41.8% recurrences are due to different genotypes. **(15)** Narendra Kumar et al. is of the view that, recurrence occurring late, after the initial treatment, are more likely to be due to reinfection. **(25)** Recurrences in Group-2b patients did not observe any pattern. Caminero et al. observed that all recurrences in their study were due to fully drug sensitive first episode strain. **(19)** The Global data suggest that 32% of the recurrence cases are due to MDR–TB infection. **(4)** Panda et al and Narendra Kumar et al. reported that 13.7% and 36%, recurrences in Cat-I, were caused by MDR-TB. **(25)** We are of the view that early recurrences occur due to the inadequate sterilization of the lesions. Chen et al. held a similar opinion. **(32)** Mitchison et al. and Mallory et al. attributed high recurrence rate to the inadequate regimen, duration of treatment, poor compliance during especially during intensive phase and initial drug resistance to one or more than one primary drugs.**(22-23,27-28)** Other Risk factors described include use of fewer than 3 drugs in initial intensive phase, shorter duration of treatment with rifampicin-containing regimen, extensive disease and cavitation, high bacterial load, male sex , the presence of concomitant disease, low body weight **(23)** and Silicosis. **(33)** HIV co-infection is definitely a risk factor for recurrence more for reinfection34 than for relapse **(35)**.

The RNTCP Technical and Operational guidelines-2016, now advocates a regular follow up of all cured and successful treatment cases every 6 months for up to 2years. **(36)** Based on the observations of the present study we suggest monthly follow up for the recurrence of symptoms in NSP cured and completed patients additionally sputum smear positive retreatment patients can also be included. Monthly follow up of the proposed target group may be more rewarding which is expected to yield >50% recurrences in 6 months and >80% recurrence in 12 months following successful completion of treatment. Chandrasekaran et al. Have also observed that the median duration of the restart of treatment in recurrence cases was approximately 7 months. **(20)** Earlier studies have also observed that the maximum recurrences were detected in 3-6 months **(16-18)** and maximum in 12 months.**(19)** Recurrences occurring thereafter are small in numbers and can be handled on felt need basis. Waiting for 6 months for the start of follow up as proposed in the RNTCP 2016 guidelines may be a late effort and needs review in the light of the above evidences and the observations of the present study too.

With the advancement in technology and wide use of mobile phones by most of the patients, monthly follow up of cured and completed sputum smear-positive for the reappearance of symptoms can be planned using mobile applications or interactive voice response system (IVRS) in the local language. Use of technology can be more authentic, cost-effective, less human dependent and capable to pick up symptomatic early. We strongly believe this strategy will dramatically reduce the quantum of tubercular infection and the opportunity of transmission of new infection in the community without putting extra financial and administrative load on the

existing RNTCP infrastructure, even in field conditions.

Limitations of the study: Statistically Significant deaths were recorded in NSP patients. Due to the insufficient data about the cause of death, the data could not be analysed.

CONCLUSION

Monthly follow up of DOTS cured and completed treatment patients, especially of NSP Cat-1 patients for the reappearance of symptoms, is advocated. Most recurrences occur in the first six months so beginning the follow up every 6 monthly, maybe a late effort. Recurrence is markedly reduced after 12 months. Since the experience is limited, more prospective studies are required to further strengthen our findings.

REFERENCES

1. Mittal C, Gupta S. Noncompliance to DOTS: How it can be decreased? Indian Journal of Community Medicine. 2011; 36:27-30.
2. Pandit S, Dey A, Chaudhuri AD, et al. Five-years experiences of the Revised National Tuberculosis Control Program in the northern part of Kolkata, India. Lung India. 2009;26:109-113.
3. Azhar GS. DOTS for TB recurrence in India: A systematic review. Lung India. 2012;29:147–153.
4. Rusen ID. Tuberculosis retreatment: a topic whose time has come. Int J Tuberc Lung Dis.2009; 13:1192
5. World health organization. Treatment of tuberculosis guidelines.4th ed. WHO/HTM/TB/2009.420. Available from: http://whqlibdoc.who.int/ Publications /2010/97892415478
6. Khatri GR. The Revised National Tuberculosis Control Programme: A Status Report On First 1,00,000 Patients. Ind.J. Tub.1999;46:157-166
7. Jyothi C, Susmitha K, Prabakaran JA. Study on the treatment out-comes in patients on dots under RNTCP in Nellore district, A.P. Nat.J.Res.Com. Med .2012;1: 01-60.
8. Chadha SL, Bhagi RP. Treatment outcome in tuberculosis patients placed under directly observed treatment short course (Dots) - A Cohort Study. Ind J. Tub. 2000; 47: 155
9. ChoudharyS,TayadeB,Keshwani P. Efficacy and treatment outcome of DOTS in RNTCP. PJMS 2012; 2:32-36
10. Dholakia Y, Danani U, Desai C. Recurrence following Directly Observed Therapy Short-course (DOTS)-A Follow up study. Ind J of Tuber. 2000; 47:233-6.
11. Sharma SK, Mohan A. Extra pulmonary tuberculosis. Indian J Med Res.2004; 120:316-53
12. Marie-Laurence Lambert, EpcoHasker, Armand Van Deun et al. “Recurrence in tuberculosis: recurrence or reinfection?” THE LANCET Infectious Diseases.2003;3:282-287 http://infection.thelancet.com
13. Panda BN, Jena J, Rai SP, Chatterji RS. Supervised chemotherapy in pulmonary tuberculosis and emergence of drug resistance in case of recurrence. Ind. J. Tub 2000; 47:163-66.
14. Das S, Chan SL, Allen BW, Mitchison DA, Lowrie DB. Application of DNA fingerprinting with IS986 to sequential mycobacterial isolates obtained from pulmonary tuberculosis patients in Hong Kong before, during and after short-course chemotherapy. Tuber Lung Dis 1993; 74: 47–51.
15. Shen X, Yang C, Wu J, Lin S, Gao X et al. Recurrent tuberculosis in an urban area in China: Recurrence or exogenous reinfection? Tuberculosis (Edinb).2017;103:97-104. PubMed PMID: 28237039.
16. Das S, Paramasivan CN, Lowrie DB, et al. IS6100 restriction fragment length polymorphism typing of clinical isolates of

Mycobacterium tuberculosis from patients with pulmonary tuberculosis in Madras, south India. Tuber Lung Dis 1995; 76: 550–54.

17. Bandera A, Gori A, Catozzi L, et al. Molecular epidemiology study of exogenous reinfection in an area with a low incidence of tuberculosis. J Clin Microbiol 2001; 39:2213–18.

18. Fox W, Ellard GA, Mitchison DA. Studies on the treatment of tuberculosis undertaken by the British Medical Research Council tuberculosis units,1946–1986, with relevant subsequent publications. Int J Tuberc Lung Dis 1999; 3: S231–79.

19. Caminero JA, Pena MJ, Campos-Herrero MI, et al. Exogenous reinfection with tuberculosis on a European island with a moderate incidence of disease. Am J RespirCrit Care Med 2001; 163: 717–20.

20. Chandrasekaran V, Gopi PG, Santha T, Subramani R, Narayanan PR. Status of re-registered patients for tuberculosis treatment under DOTS programme. Indian J Tuberc 2007;54:12-6.

21. Mehra RK, Dhingra VK, Nish A et al. Study of recurrence and failure cases of CAT I retreated with CAT II under RNTCP--an eleven year follow up. Ind. J Tuberc. 2008;55:188-91. PubMed PMID: 19295105.

22. Thomas A, Gopi P.G.,Santha T, Chandrasekaran V,Subramani R, SelvakumarN et al. Predictors of recurrence among pulmonary tuberculosis patients treated in a DOTS programme in South India. Int J Tuberc Lung Dis. 2005;9 :556-61. Pub Med PMID:15875929

23. Cox HS, Morrow M, Deutschmann PW. Long-term efficacy of DOTS regimens for tuberculosis: systematic review. BMJ : British Medical Journal. 2008;336:484-487. doi:10.1136/bmj.39463.640787.BE.

24. Yatin D, Danani U, Desai C. Recurrence following directly observed therapy short course (DOTS): a follow-up study. Indian J Tub 2000; 47: 233-6.

25. Narendra Kumar Narahari, Sudhir KumarVujhini. Drug Sensitivity Pattern among Category–I Recurrence Cases of Pulmonary Tuberculosis and Its Correlation with Pre- treatment Sputum and Radiological Status.MRIMS Journal of Health Sciences 2016;4:166 - 170

26. Daniel D and Bernt L.Tuberculosis recurrence in smear-positive patients cured under DOTS in southern Ethiopia: retrospective cohort study. BMC Public Health.2009;9:348

27. Mitchison DA, Nunn AJ. Influence of initial drug resistance on the response to short-course chemotherapy of pulmonary tuberculosis. Am Rev Respir Dis 1986; 133: 423–30. 9

28. Mallory KF, Churchyard GJ, Kleinschmidt I, De Cock KM, Corbett EL. The impact of HIV infection on recurrence of tuberculosis in South African gold miners.Int J Tuberc Lung Dis 2000; 4: 455–62. 10

29. Cao JP, Zahang LY, Zhu JQ et al. Two year follow-up of directly observed intermittent regimens for smear-positive pulmonary tuberculosis in China. Int. Journal of Tuberculosis & Lung diseases 1998;2:360-364

30. De Saja. High recurrence rate in RNTCP: An increasing concern and time to intervene. Lung India 2013;1: 85-86

31. Sahadevan R, Narayanan S, Paramasivan CN, Prabhakar R, Narayanan PR. Restriction fragment length polymorphism typing of clinical isolates of Mycobacterium tuberculosis from patients with pulmonary tuberculosis in Madras, India, by use of direct-repeat probe. J Clin Microbiol 1995; 33: 3037–39.

32. Chan-Yeung M, Noertjojo K, Chan SL, Tam CM. Sex differences in tuberculosis in Hong Kong. Int J Tuberc Lung Dis 2002; 6: 11–18.

33. Rees D, Murray J. Silica, silicosis and tuberculosis. Int J Tuberc Lung Dis.2007 May;11(5):474-84. Review. PubMed PMID: 17439668.

34. Sonnenberg P, Murray J, Glynn JR, Shearer S, Kambashi B, Godfrey-Faussett P. HIV-1 and recurrence, recurrence, and reinfection of tuberculosis after cure: a cohort study in South African

35. Johnson JL, Okwera A, Nsubuga P, et al. Efficacy of an unsupervised 8-month rifampicin-containing regimen for the treatment of pulmonary tuberculosis in HIV-infected adults. Uganda-Case Western ReserveUniversity Research Collaboration.Int J Tuberc Lung Dis 2000; 4: 1032–40.14

36. Revised National TB Control Program, Technical and Operational Guidelines for Tuberculosis Control in India 2016, page 53. Published by Central TB Division, Directorate General of Health Services, Ministry Of Health & Family Welfare , New Delhi, India downloaded from http://tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=4573&lid=317 dated 13.09.2017

Annexure-1
For the use in case of symptomatic

Name Age/Sex
Address
Mobile; Yes/No (If yes mobile no……)
Date……
Investigation

Investigation type	Date/ Report	Date/Report	Date/Report
Sputum Smear for AFB			
Blood; TLC/DLC			
Blood sugar (R)			
HIV status			
Biochemistry;			
B. Urea/ S.Creatinine			
S. bilirubin			
SGOT/PT			
Urine routine			
Any Other			

X-ray Chest PA view report

Report of any other imaging study done

Remark

Signature with Name

Date