International Journal of Advances in Medicine
Ramesh PM et al. Int J Adv Med. 2018 Jun;5(3):561-565
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20181663

Original Research Article

Impact of drug susceptibility on treatment outcome in sputum smear positive pulmonary tuberculosis patients receiving category-II regimen in RNTCP under field conditions in an urban setting

Ramesh P. M.*, Saravanan M.

Department of Pulmonary Medicine, Kilpauk Medical College, Chennai, Tamil Nadu, India

Received: 31 March 2018
Accepted: 16 April 2018

***Correspondence:**
Dr. P. M. Ramesh,
E-mail: pmrmdchest2@gmail.com

ABSTRACT

Background: The study was conducted with the aim to evaluate the pre-treatment drug susceptibility profile and to assess the influence of drug resistance on treatment outcome among patients treated with category- II (cat- II) regimen under programme conditions.
Methods: This study was conducted on 58 smear positive patients with history of previous anti-tuberculosis treatment for more than one month, comprising cases of 'Failure', 'Treatment after Default' (TAD) and 'Relapse'. They received cat- II regimen in Chennai Corporation, RNTCP (revised National tuberculosis control programme) centers from July 2006 to September 2006 and they were monitored upto July 2007 as per RNTCP guidelines to assess the outcome of cat-II treatment by sputum smear status.
Results: Male dominance (n=40) was seen in the study participants. Most common age group affected was 35-44 years (n=20). Out of 57 cases, 50.9% cases come under 'Relapse', 26.3% arises from 'TAD' and 22.8% cases were from 'Failure'. After completion of treatment with cat-II regimen, out of 57 patients 33 patients were cured and 11 cases were into the category of failure, 10 patients were defaulted during treatment and 3 were died.
Conclusions: Besides, the low treatment efficiency in MDR-TB cases, cat- II regimen was effective in sensitive and INH resistant cases.

Keywords: Category- II regimen, Drug susceptibility, RNTCP

INTRODUCTION

Tuberculosis (TB) is considered as one of the major health problems causing mortality in adults in the developing countries.[1] Initially the treatment recommended for TB was with short-course (DOTS) strategy by the World Health Organization which includes a combination of rifampicin-isoniazide-pyrazinamide-ethambutol.[2]

But the increased availability and haphazard use of Rifampicin, both in public and private sectors, from mid1980's onwards has led to increasing proportions of multi drug resistant tuberculosis (MDR-TB).[3] Management of such resistant cases has stood a therapeutic dilemma to developing countries with infrequent resources.[4]

In the year 1982, the revised National tuberculosis control programme (RNTCP) concluded that the previously implemented National tuberculosis control program (NTCP) suffered from managerial weakness, inadequate funding, an over-reliance on X-rays, non-standard treatment regimens, low rates of completion of treatment and a lack of systematic information on treatment outcome.[5,6] With the recommendations of an

expert committee, a revised strategy to control TB was established in 1993, and the RNTCP was started in 1997, and geographic coverage of more than 97% was achieved by the end of 2005.[7]

As per RNTCP programme, new smear positive pulmonary tuberculosis patients was treated with category-I regimen and the outcome has been reported to be good with a success rate of 83% or greater at national level but for previously treated patients, the success rate to the re-treatment regimen (cat-II) was low (71%) and among patients typed as 'Failure' and treated with re-treatment regimen, risk of subsequent failure was higher, compared to other types.[8,9]

The level of drug resistance in the community especially in cases of MDR-TB posing a greatest challenge to the clinicians regarding the effectiveness of cat - II regimen for re-treatment cases, especially those with failures.

It has been suggested that they may be treated with a stronger regimen since such cases are likely to harbor drug resistant organisms.

The aim of the present study was to evaluate the pre-treatment drug susceptibility profile and to assess the influence of drug resistance on treatment outcome among patients treated with cat-II regimen under programme conditions.

METHODS

This was an prospective study that included 58 smear positive patients with history of previous anti-tuberculosis treatment for more than one month, comprising cases of 'Failure', 'Treatment after Default' and 'Relapse'.

These patients were started on the category - II regimen in Chennai corporation, RNTCP centers from July 2006 to September 2006 after getting approval from Medical ethics committee.

From these patients sputum was collected for sputum smear examination and for culture and sensitivity before starting cat-II regimen and they were monitored upto July 2007 as per RNTCP guidelines to assess the outcome of cat- II treatment.

A patient, who was HIV infected or diabetic, was excluded from the study. Hence, sputum smear was examined in 57 patients using Ziehl-Neelson method for the presence of acid-fast Mycobacteria tuberculosis.[10] Outcome of cat-II was concluded by sputum smear status according to RNTCP guidelines.[11]

Definitions of various outcomes

Cured: Initially smear-positive patient who has completed treatment and had negative sputum smears, on at least two occasions, one of which was at completion of treatment

Treatment completed

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 TB patient who has received a full course of treatment and has not become smear positive during or at the end of treatment (or) extra-pulmonary TB patient who has received a full course of treatment and has not become smear-positive during or at the end of treatment.

Died

Who died during treatment, regardless of cause.

Failure

Any tuberculosis patient who is smear-positive at 5 months or more after starting treatment (or) a patient who was treated with cat III but who became smear-positive during treatment.

Defaulted

Who, at any time after registration, has not taken anti- TB drugs for 2 months or more consecutively.

Transferred out

Who has been transferred to another tuberculosis unit/district and his/her transferred out treatment results are not known.

Data Analysis

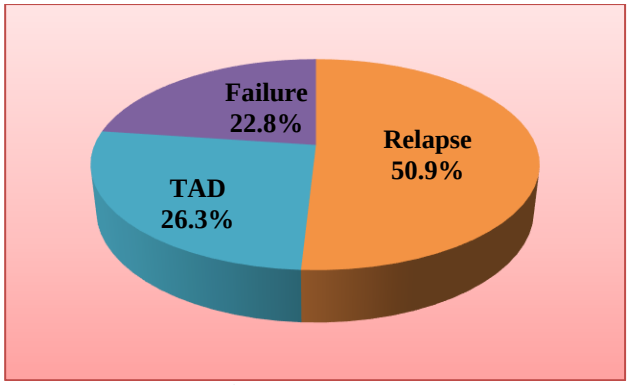
The data was entered into the Microsoft Excel work sheet and it is analyzed using SPSS software.

RESULTS

Total 57 patients that were registered under cat- II were taken up for study. Their demographic and clinical details were given in Table 1. More number of males (n=40) had registered under cat - II than females (n=17).

Table 1: Age and sex distribution of study participants.

Age in years	Female	Male	Total
<25	3	4	7
25-34	7	11	18
35-44	5	15	20
45-54	1	7	8
>55	1	3	4
Total	17	40	57



TAD- Treatment under default.

Figure 1: Purpose for starting CAT– II regimen.

Out of 57 cases, 50.9% (n=29) cases comes under 'Relapse', 26.3% (n=15) arises from 'TAD' and 22.8% (n=13) cases were from 'Failure' category as shown in Figure 1.

Table 2 presents the reasons for undergoing the treatment with cat- II regimen and its related outcome. Out of 57, 29 patients were under relapse.

Of them, 82.8% (n=24) of the patients were Cured, 6.9% (n=2) of the patients had Failure; another 6.9% (n = 2) of the patients were Defaulted at the end of cat- II and 1 patient Died during treatment.

Table 2: Reason for starting CAT– II treatment and its outcome related to drug sensitivity pattern (n=57).

Drug sensitivity	Cured		Defaulted		Failure		Died		Total	
	No	%	No	%	No	%	No	%	No	%
Relapse										
Sensitive	20	95.2	1	4.8	-	-	-	-	21	72.4
INH-resistant	3	50.0	1	16.7	1	16.7	1	16.7	6	20.7
MDR	1	50.0	-	-	1	50.0	-	-	2	6.9
Total	24	82.8	2	6.9	2	6.9	1	3.4	29	100.0
TAD										
Sensitive	5	55.6	4	44.4	-	-	-	-	9	60.0
INH-resistant	1	33.3	1	33.3	1	33.3	-	-	3	20.0
MDR	-	-	2	66.6	1	33.3	-	-	3	20.0
Total	6	40.0	7	46.7	2	13.3	-	-	15	100.0
Failure										
Sensitive	-	-	-	-	-	-	1	100.0	1	7.7
INH-resistant	1	33.3	1	33.3	-	-	1	33.3	3	23.0
MDR	2	22.2	-	-	7	77.8	-	-	9	69.3
Total	3	23.1	1	7.7	7	53.8	2	15.4	13	100.0
Grand total										
Sensitive	25	80.7	5	16.1	-	-	1	3.2	31	54.5
INH-resistant	5	41.6	3	25	2	16.7	2	16.7	12	21.0
MDR	3	21.4	2	14.3	9	64.3	-	-	14	24.5
Total	33	57.9	10	17.5	11	19.3	3	5.3	57	100.0

INH- Isoniazid, MDR- Multi drug resistant.

Among 15 TAD patients, 46.7% (n=7) of them again get Defaulted during cat II and 40% (n=6) of the patients had Cure and 13.3% (n=2) of the patients were declared failed. Regarding patients who had failure in cat– I (n=13), 7 patients (53.8%) again had Failure in the cat- II regimen and 3 patients (23%) had Cure with cat - II. Among died patients (n=3), two patients were Failure with cat– I; 1 patient had relapse with cat- I.

After completion of treatment with cat- II regimen, out of 57 patients, 57.9% (n=33) patients were cured and 19.3% (n=11) cases were fell into the category of failure and 17.5% (n=10) patients were defaulted during treatment and 3 (5.2%) were died (Table 3).

Table 3: Outcome of cat- II regimen.

Outcome of cat- II regimen	Number of patients (n=57)	%
Cured	33	57.9
Defaulted	10	17.5
a. Alcoholic	6	10.5
b. Migrated	2	3.5
c. Work pattern	2	3.5
Failure	11	19.3
Died	3	5.3
a. Severe PT	2	3.5
b. Road traffic accident	1	1.8

Of the 14 MDR-TB patients, on treatment with cat- II regimen, 22% (n=3) of the patients had successful treatment outcome; 14% (n=2) of the patients were defaulted and 64.3% (n=9) of the patients were registered as failure (Figure 2).

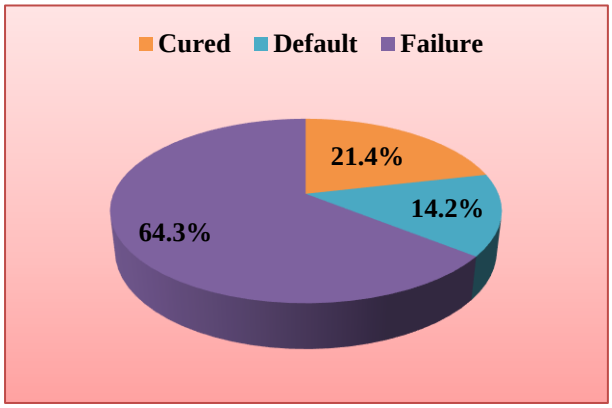


Figure 2: Outcome of MDR-TB patients according to type of cases.

DISCUSSION

In the present study, totally 57 consecutive smear positive patients of relapse, failure, TAD cases who were registered in cat - II from July 2006 to September 2006 in Chennai corporation RNTCP centre were included and referred to TRC, Chetpet for pre-treatment sputum AFB culture and drug sensitivity And these patients were monitored consecutively till the end of cat- II regimen and their outcome was documented according to sputum smear status as per RNTCP guidelines.

In our study, among 57 patients registered under cat-II, 31 patients (54.5%) harboring fully susceptible bacilli, 10 patients (21%) harboring resistant but non-MDR bacilli, and 14 patients (24.5%) had MDR-TB.

These observations were similar to the findings made by Joseph et al.[12]

In his study out of 572 cases, 431 patients produced positive cultures. Of them, 254 (59%) patients' harbored sensitive bacilli, 128 (30%) patients had resistant but non-MDR bacilli, 49 (11%) patients had MDR-TB.

In the study of Joseph et al, among 49 patients with MDR-TB, 13 (27%) had a favorable outcome and failure rate was highest among patients with MDR-TB ($p<0.05$).12 An analysis of the present study also demonstrated similar trends. Of the 14 MDR-TB patients, 21.4% (n=3) of the patients had cure; 14.3% (n=2) of the patients were defaulted and 64.3% (n=9) of the patients had failure with cat II regimen.

The overall favorable treatment outcome in our study at end of cat– II regimen was 57.9% (cured, n=33) with TAD in 10 patients (17.5%) during treatment, failure in 11 patients (19.3%) and death in 3 patients (5.3%). This was in accordance with the findings of Sophia Vijay et al.[13] Out of 268 patients, the overall favorable treatment outcome was 39.8%. 'Death' among re treatment cases was 3.1%.

Similarly, in retrospective cohort study of patients enrolled into the WHO/IUALTD global projects on drug resistance surveillance in 6 countries, Espinal et al has reported that of the 876 re-treatment cases, 44.5% were drug resistant, including 19% of MDR-TB.14 Among them, 57% had a successful outcome, 6% died and 14% failed. And failure rates among re treatment cases were higher in those with MDR-TB and with Isoniazid resistance other than multi-drug resistance.

A report from Malawi has reported a treatment outcome of 65% for patients with recurrent TB, 81% of cat - II patients had susceptible organisms and MDR-TB was observed only in 4% of cases.[15]

The treatment compliance is the most important factor for the effective outcome of a regimen. Moreover, the resistance with cat-I regimen, particularly in cases of MDR-TB, was strongly associated with prior TB treatment of 20 weeks. This might be by the result of TAD, or poor quality of tuberculosis services with unsupervised SCC regimen presented in the earlier study area.

CONCLUSION

The tuberculosis bacilli which retains their susceptibility to anti-tuberculous drugs, was relatively high in cases of 'Relapse' than 'TAD' and 'Failure' cases. The cure rate of patients undergoing with cat- II regimen with fully susceptible and resistant but non MDR-TB, was relatively higher than the patients who are having multi drug resistant tuberculosis (MDR-TB).

21.4% of the patients who turned out to be MDR-TB got cured and converted at the end of intensive phase and remained smear negative showing the efficiency of 5 drugs in intensive regimen and in vitro drug susceptibility.

Regarding the patients who failed in treatment with cat-II, future thought for early switching over to DOTS plus by planning drug sensitivity testing (DST) at the failure of sputum smear conversion at 3 month of intensive phase itself will prevent default/failure/mortality. Initial DST in retreatment cases at least in treatment failure cases will benefit major portion of MDR-TB cases from getting lost to RNTCP.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. TB′s History. Available from: http://www.library.thinkquest.org/C0126375/tb_in_the_world.htm. Accessed on 26 December 2012.
2. Han T. Effectiveness of standard short-course chemotherapy for treating tuberculosis and the impact of drug resistance on its outcome. Int J Evid Based Healthc. 2006;4:101-17.
3. Trivedi SS, Desai SE. Primary anti TB resistance and acquired Rifampicin resistance in Gujarat. India Tubercle. 1988;69:37.
4. Kuadan C, Bercion R, Jifon G, Cunin P, Blackett KN. Acquired anti-TB drugs resistance in Yaounde, Cameroon. Int J Tuberc Lung Dis. 2000;4:427.
5. Verma R, Khanna P, Mehta B. Revised national tuberculosis control program in India: The need to strengthen. Int J Prev Med. 2013;4:1-5.
6. Khatri GR. The revised national tuberculosis control programme: A status report on first 1,00,000 patients. Indian J Tuberc. 1999;46:157-66.
7. About RNTCP. Available at: http://www.tbcindia.nic.in/RNTCP.html. Accessed on 26 December 2012.
8. Khatri GR, Frieden TR. Controlling tuberculosis in India. New Eng J Med. 2002;347:1420-6.
9. TB India. RNTCP Status report. Central TB Division, Directorate General of Health Services. Ministry of Health and FamilyWelfare, Nirman Bhavan, New Delhi, 2004.
10. Ziehl–Neelsen technique. Available at: Online Microbiology Notes". Online Microbiology Notes. Accessed on 29 November 2017.
11. Revised National Tuberculosis Control Programme Technical guidelines for TB control. Central TB Division, Directorate General of Health Services, Nirman Bhavan, New Delhi, India, 1997.
12. Joseph P, Chandrasekaran V, Thomas A, Gopi PG, Rajeswari R, Balasubramanian R, et al. Influence of drug susceptibility on treatment outcome and susceptibility profile of ‘failures’ to category ii regimen. Indian J Tuberculosis. 2006;53:141-8
13. Vijay S, Balasangameshwara VH, Jagannatha PS, Saroja VN, Shivashankar B, Jagota P. Re-Treatment outcome of smear positive tuberculosis cases under dots in Bangalore City. Indian J Tuberculosis. 2002;49:199-204.
14. Espinal MA, Laserson K, Camacho M, Fusheng Z, Kim SJ, Tlali RE, et al. Determinants of drug resistant tuberculosis: analysis of 11 countries. Int J Tuberc Lung Dis. 2001;5:887.
15. Salaniponi FM, Nyirenda TE, Kemp JR, Squire SB, Godfrey-Faussett P, Harries AD. Characteristics, management and outcome of patients with recurrent tuberculosis under routine programme conditions in Malawi. Int J Tuberc Lung Dis. 2003;7:948-52.

Cite this article as: Ramesh PM, Saravanan M. Impact of drug susceptibility on treatment outcome in sputum smear positive pulmonary tuberculosis patients receiving category-II regimen in RNTCP under field conditions in an urban setting. Int J Adv Med 2018;5:561-5.