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A Comparative study on Efficacy of Antituberculosis drugs in Immunocompetent and Immunocompromised Sputum Positive Pulmonary Tuberculosis Patients

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Abstract

Incidence of HIV and DM are increased nowadays. Both groups are more chance for TB infection. Efficacy of DOTS regimen is find out in both groups in the study**.** To compare the rate of sputum conversion in new smear positive pulmonary tuberculosis Immunocompetent and Immunocompromised patients. The study was conducted at RNTCP (Revised National Tuberculosis Control Programme) centre, Madurai Medical College and Rajaji Hospital, Madurai, Tamilnadu. The study was a prospective study and consists of totally 100 patients of smear positive Pulmonary Tuberculosis (50 Immunocompetant patients and 50 Immunocompromised patients) (category- I) irrespective of age and sex. In the present study, among immunocompetent patients, 42(84%) patients became smear negative at the end of the 2nd month, 48(96%) patients became sputum smear negative at the end of 3rd month. Among immunocompromised patients, 45(90%) patients became smear negative at the end of 2nd month, 50(100%) patients became sputum smear negative at the end of 3rd month. In the present study, sputum conversion at the end of third month was 96% in immunocompetant patients and 100% in immunocompromised patients. $P > 0.05$ hence was not statistically significant. This study demonstrates that HIV – seropositive status and DM are not a principal factor in delaying sputum conversion.

Key-Words: DOTS- Directly Observad Treatment Short-course

Introduction

Tuberculosis remains a major public health problem worldwide. It has been estimated that someone in the world is newly infected with tuberculosis every second, nearly 1% of the world population is infected with TB every year and overall, one third of the world population is infected with mycobacterium tuberculosis [1, 2, 3]. India is the highest TB burden country accounting for one fifth (21%) of the global incidence. India is 17th among 22 high burden countries in term of TB incidence rate. (Source: WHO global TB report 2010) [4]. The prevalence of TB in the country has reduced from 568/100,000 population in 1990 to 249/100,000 population by the year 2010 as per the WHO Global TB Report, 2010[4].

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In healthy people, infection with Mycobacterium tuberculosis often causes no symptoms, since the person's immune system acts to "wall off" the bacteria [4]. People with HIV and TB infection are much more likely to develop TB. Compared to an individual who is not infected with HIV, a person infected with HIV has approximately, a five times increased lifetime risk of developing TB. TB is the most common life threatening opportunistic infection associated with HIV [5,6]. TB accelerates the progression of HIV as evidenced by a 6 to 7 fold rise in HIV viral load in the dually infected as compared to HIV person without TB[6].

The risk for developing TB disease is also higher in persons with diabetes, other chronic debilitating disease leading to immune-compromise, poor living conditions, tobacco smokers etc[4]. TB is two to seven times more common in diabetic patients [7, 8]. Nearly 30% of diabetic patient have tuberculosis [9, 10, 11] and it has been seen that TB is the most common (5.9%) complicating illness in diabetics [12]. In developing

countries-like ours, diabetes is an independent and significant risk factor for TB, the risk of TB attributable to diabetes being equivalent to that attributable to HIV infection(~25%) [6].

The Revised National TB Control Programme (RNTCP), based on the internationally Recommended Directly Observed Treatment Short-course (DOTS) strategy, was launched in1997 expanded across the country in a phased manner with support from the World Bank and other development partners. The programme has now revised its categorization of patients from the earlier 4 categories (Cat I, Cat II, Cat III and Cat IV) to 3 categories (New cases-Cat I, Previously treated cases-Cat II and Cat IV) based on the recommendations of experts and endorsement by National Task Force for Medical colleges[4].

To compare the rate of sputum conversion in both new smear positive pulmonary tuberculosis Immunocompetent and Immunocompromised patients.

Material and Methods

The study was conducted at RNTCP centre, Madurai Medical College and Rajaji Hospital, Madurai, Tamilnadu. Institutional ethical clearance was obtained from the ethical committee, Government Rajaji Hospital, Madurai. Written informed consent was obtained from all patients, The study was a prospective study and consists of totally 100 patients of smear positive Pulmonary Tuberculosis (50 Immunocompetant patients and 50 Immunocompromised patients) (category-I) irrespective of age and sex.

INCLUSION CRITERIA:

(a) For immunocompetent group:

1. New sputum smear positive pulmonary Tuberculosis patients.

(b) For immunocompromised group:

1. New smear positive pulmonary tuberculosis patients with Diabetes mellitus.
2. New smear positive pulmonary tuberculosis patients with Human Immunodeficiency Virus infection.

EXCLUSION CRITERIA:

1. Chronic liver diseases.

2. Chronic Renal failure.

3. Pregnant and Lactating Women.

DRUG REGIMEN:

The selected patients were administered antitubercular drug under DOTS regimen according to category-I ($2H_3R_3Z_3E_3$&$4H_3R_3$). (H-Isoniazid, R-Rifampin, Z-Pyrazinamide, E-Ethambutol)

SPUTUM SAMPLING:

Two sputum samples were collected over two consecutive days,

- Spot sample on the first day.
- One early morning sample on the second day.

METHODOLOGY

50 patients of New Sputum Smear positive Pulmonary Tuberculosis with Immunocompromised state & 50 patients of New Sputum Smear positive pulmonary tuberculosis with Immunocompetant state were selected. The age & sex distribution of immunocompetent patients belonged to 1st, 3rd 4th decades, 64% were males and 36% were female with ratio of 2:1.2. In immunocompromised patients, 88% belonged to 3rd, 4th, 5th decades with 64% were males and 36% were female with ratio of 2:1.2**. (Table-1).**

In Immunocompromised group, 23 patients were HIV infected and remaining 27 patients were Diabetic **(Fig-I).** HIV infected patients were only on Antitubercular drugs & not on Antiretroviral therapy. In our study, all HIV positive patients` CD4 count was above 350 cells. All diabetic patients were on good diabetic control throughout the study period.

In immunocompetant group, 3+ sputum grading was seen in 19 baseline patients, 2+ sputum grading was seen in 4 baseline patients, 1+ sputum grading was seen in 26 baseline patients,. Scanty sputum smear was seen in 1 baseline patient.

In immunocompromised group, 3+ sputum grading was seen in 15 baseline patients, 2+ sputum grading was seen in 10 baseline patients, 1+ sputum grading was seen in 20 baseline patients. Scanty sputum grading smear was seen in 5 baseline patients **(Table-2)**

Both groups of patients were treated with category-I-RNTCP Regimen ($2H_3R_3Z_3E_3$). Both groups of patients were examined with Sputum AFB Smear, after completing two months of treatment. The intensive phase of treatment consisting of $H_3R_3Z_3E_3$ was continued for another 4 weeks if the patients were sputum positive at the end of second month as per DOTS [13]. After third month, these groups of smear positive patient were examined with 2 sample sputum AFB smear for sputum conversion.

The conversion rate at 2-3 months *(defined as the proportion of initially smear positive patient with negative smears out of the total who started the treatment)* is a good operational indicator [14]. It shows the capacity of the program to maintain patients on treatment, obtain smear samples, and eliminate source of infection, and it is an early surrogate of the treatment outcome indicator [14]. The conversion rate was analyzed statistically.

Results and Discussion

The present study shows decreased infectivity from baseline at the end of 2nd month and 3rd month for both groups.

SPUTUM CONVERSION: **(Table 3) (Figure 2)**

- *3+ baseline grading :*

Out of 19 immunocompetent patients, At the end of 2nd month - 14 (73%) patients → smear negative, & 5(26%) patients →1+ grading. At the end of 3rd month, 18 (95%) patients → smear negative

Out of 15 immunocompromised, At the end of 2nd month -14 (93%) patients → smear negative & 1(7%) patient → scanty. At the end of 3rd month, 15(100%) patients → smear negative

- *2+ baseline grading :*

Out of 4 immunocompetent patients, At the end of 2nd month -2(50%) patients → 1+ grading & 2(50%) patients smear→ negative

At the end of 3rd month, 3(75%) patients → smear negative

Out of 10 immunocompromised patients , At the end of 2nd month, 1(10%) patient → 1+ grading , 1(10%) patient → scanty& 8 (80%) patients → smear negative.

At the end of 3rd month, 10(100%) → smear negative.

- *1+ baseline grading :*

Out of 26 immunocompetent patients, At the end of 2nd month, 1(4%) patient → scanty, 25(96%) patients → smear negative, At the end of 3rd month, 26 (100%) patients → negative .

Out of 20 immunocompromised patients , At the end of 2nd month, 1(5%) patient → scanty, 19 (95%) patients → negative, At the end of 3rd month, 20(100%) patients → negative.

- *Scanty baseline grading :*

1 immunocompetent patient, At the end of 2nd month, 1(100%) patient → negative

Out of 5 immunocompromised patients , At the end of 2nd month,1(20%) patient → persistently scanty, 4(80%) patients → smear negative

At the end of 3rd month, 5(100%) patients → smear negative

SPUTUM CONVERSION RATE

In the present study, sputum conversion i.e from smear positive to smear negative at the end of the 2nd month & 3rd month is 84% & 96% in immunocompetent patients, 90% & 100% in immunocompromised patient**.(Fig-3)**

Sputum conversion rate[14] = " Number of new smear-positive pulmonary TB cases registered in a specified period that are smear negative at the end of the initial phase of treatment"

----------X 100 " Total number of new smear-positive pulmonary TB cases registered for treatment in the same period "

In the present study of 50 smear positive pulmonary tuberculosis with immunocompetent cases, 84% patients at the end of 2nd month and 96% patients at the end of 3rd were smear negative. **Fig-3(a)**

Sputum conversion rate = 96/100 × 100 =96%

50 smear positive pulmonary tuberculosis with immunocompromised cases, 90% patients at the end of 2nd month and 100% patients at the end of 3rd month were smear negative. **Fig-3(b)**

Sputum conversion rate = 100/100 × 100 =100%

One way analysis of variance(ANOVA) showed that there was no significant difference in the bacteriological outcome responses to TB chemotherapy between the combined groups of immunocompetent sputum smear positive tuberculosis patients and immunocompromised smear positive tuberculosis patients. The P value at two months and at three months was 0.954 and 0.166 respectively. These were greater than the 0.05 critical value, hence were not statistically significant.

In the present study, the age & sex distribution of immunocompetent patients belonged to 1st, 3rd 4th decades, 64% were males and 36% were female with ratio of 2:1.2. In immunocompromised patients, 88% belonged to 3rd, 4th, 5th decades with 64% were males and 36% were female with ratio of 2:1.2**.** More males were infected than females, possibly because of low sputum positivity among women with TB. Some women could not produce the required quantity of sputum leading to false negative tests, which was more common in women than men[15]

In immunocompromised group, 23 patients are HIV infected and remaining 27 patients are Diabetic **(Fig-I).** HIV infected patients were only on Antitubercular drugs & not on Antiretroviral therapy. Antituberculous treatment remains a central priority for the management of HIV positive TB patients and should not be compromised by ART. WHO (2006) recommended completion of TB therapy before the commencement of ART unless there is a high risk of HIV disease progression and death during the course of TB treatment (CD4 counts <350 cells/µL or the presence of disseminated TB) [16]. In our study, all HIV positive patients` CD4 count was above 350 cells/µL. All diabetic patients were on good diabetic control throughout the study period.

The best way to monitor the treatment result of a pulmonary tuberculosis sputum positive case is to check for the conversion of sputum from smear positive to smear negative [17-25]. Among 50 immunocompetent sputum positive pulmonary

tuberculosis (category-I) patients, 42(84%) patients became smear negative at the end of the 2nd month, 48(96%) patients became sputum smear negative at the end of 3rd month. Among 50 immunocompromised sputum positive pulmonary tuberculosis (category-I) patients, 45(90%) patients became smear negative at the end of 2nd month, 50(100%) patients became sputum smear negative at the end of 3rd month.

Sputum conversion at the end of third month was 96% in immunocompetent patients and 100% in immunocompromised patients.

One way analysis of variance(ANOVA) showed that there was no significant difference in the bacteriological outcome responses to TB chemotherapy between the combined groups of immunocompetent sputum smear positive tuberculosis patients and immunocompromised smear positive tuberculosis patients. The 'P' Value of sputum conversion rate in both groups is 0.943, as not statistically significant.

So kwange et al from *kenya* (Jan-2010) observed sputum conversion after the 2nd month intensive phase was 92% in HIV negative TB patients and 88% in HIV patients [26]

V.V.Banurekha et al from *TRC, ICMR, chennai* (November 2007) showed sputum conversion (culture) after the second month was 88% in DM-TB patients & 93% in HIV-TB patients [27].

Conclusion

In the present study, age distribution of 50 immunocompetent patients showed that majority of the patients (72%) belonged to 1st 3rd 4th decades with mean age of 34 years. In 50 immunocompromised patients, majority of the patients (88%) belonged to 3rd, 4th, 5th decades with mean age of 41 years.

In the present study, among 50 cases of immunocompetent with sputum positive pulmonary tuberculosis(category-I) patients, 42(84%) patients became smear negative at the end of the 2nd month,48(96%) patients became sputum smear negative at the end of 3rd month. 50 cases of immunocompromised with sputum positive pulmonary tuberculosis (category-I) patients, 45(90%) patients became smear negative at the end of 2nd month, 50(100%) patients became sputum smear negative at the end of 3rd month.

One way analysis of variance(ANOVA) showed that there was no significant difference in the bacteriological outcome responses to TB chemotherapy between the combined groups of immunocompetent sputum smear positive tuberculosis patients and immunocompromised smear positive tuberculosis patients. Directly Observed Treatment is an effective intervention for improving adherence to tuberculosis treatment programme in both immunocompetent and immunocompromised group. This study demonstrates that HIV-seropositive status and DM are not a principal factor in delaying sputum conversion among patients receiving intensive phase tuberculosis treatment.

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Table 1: Demographic pattern

Age in years	Immunocompetant group (M+F)		Immunocompromised group (M+F)	
	M	**F**	**M**	**F**
11-20	8%	14%	0 %	0%
21-30	6%	6%	2%	4%
31-40	18%	8%	20%	6%
41-50	22%	2%	18%	16%
51-60	8%	6%	18%	10%
61-70	2%	0%	6%	0%
Total	64%	36%	64%	36%

Table 2: Grading of sputum at baseline

Sputum grading	Immunocompetent - *Base line*	Immunocompromised - *Base line*
3+	19	15
2+	4	10
1+	26	20
Scanty	1	5
Negative	0	0

Table 3: Sputum conversion from baseline and at the end of 2nd, 3rd Month

Immunocompetent				**Immunocompromised**			
Baseline	Sputum conversion	Sputum Conversion at 2nd month	Sputum conversion at 3rd month	Baseline	Sputum conversion	Sputum Conversion at 2nd month	Sputum conversion at 3rd month
19	3+ to 2+	0	0	15	3+ to 2+	0	0
	3+ to 1+	5 (26%)	1		3+ to 1+	0	0
	3+ to SC	0	0		3+ to SC	1 (7%)	0
	3+ to Neg	14 (73%)	4 (95%)		3+ to Neg	14 (93%)	1 (100%)
4	2+ to 1+	2 (50%)	1	10	2+ to 1+	1 (10%)	0
	2+ to SC	0	1		2+ to SC	1 (10%)	0
	2+ to Neg	2 (50%)	1 (75%)		2+ to Neg	8 (80%)	2 (100%)
26	1+ to SC	1 (4%)	0	20	1+ to SC	1 (5%)	0
	1+ to N	25 (96%)	1 (100%)		1+ to N	19 (95%)	1 (100%)
1	SC to SC	0	0	5	SC to SC	1 (20%)	0
	SC to N	1 (100%)	0		SC to N	4 (80%)	1 (100%)
Total 50		50		Total 50	50	50	

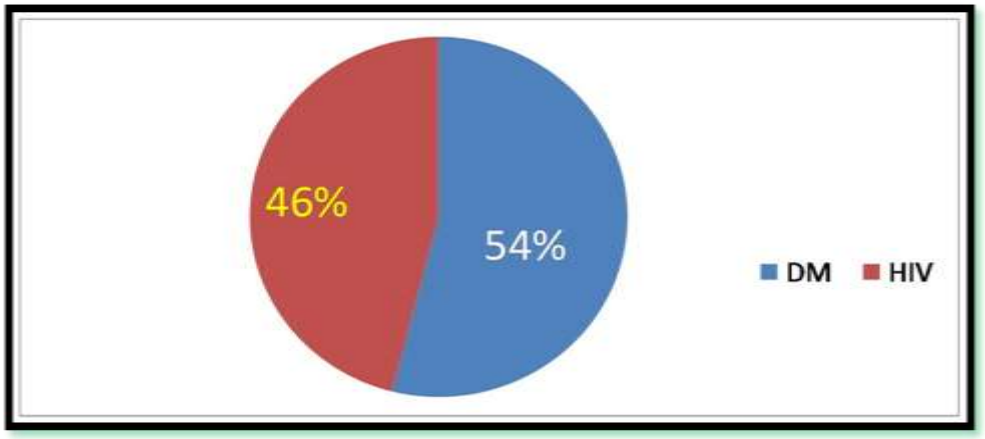


Fig. 1: Disease pattern

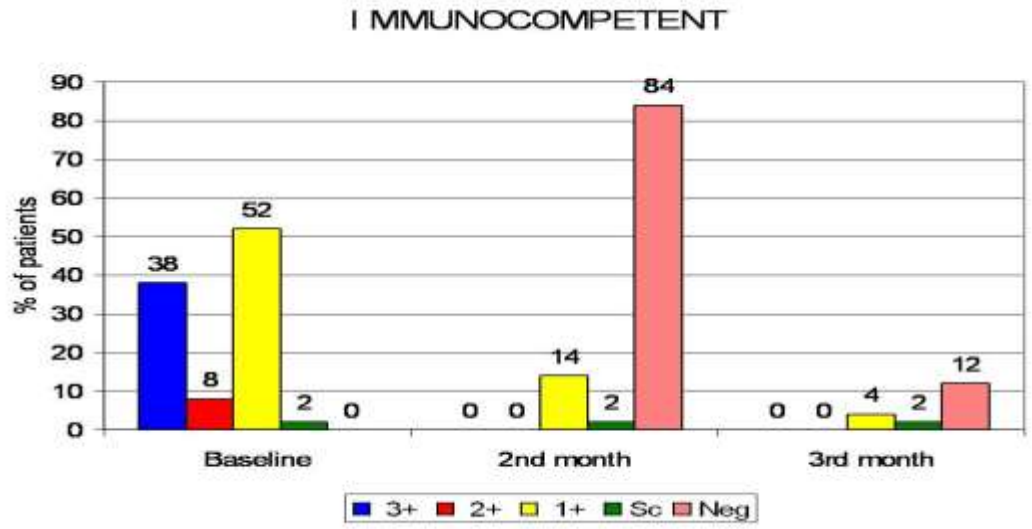


Fig. 2: Bar diagram showing sputum Positivity at baseline, at the end of 2nd, 3rd month

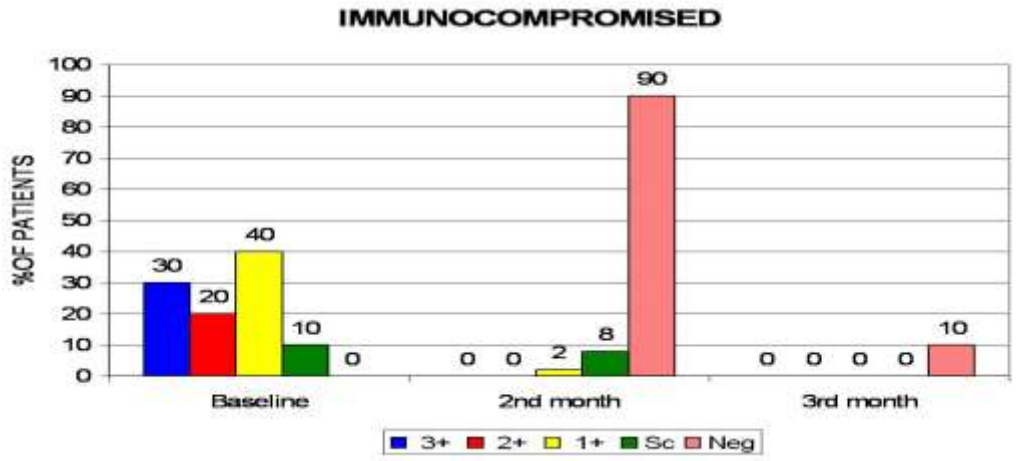
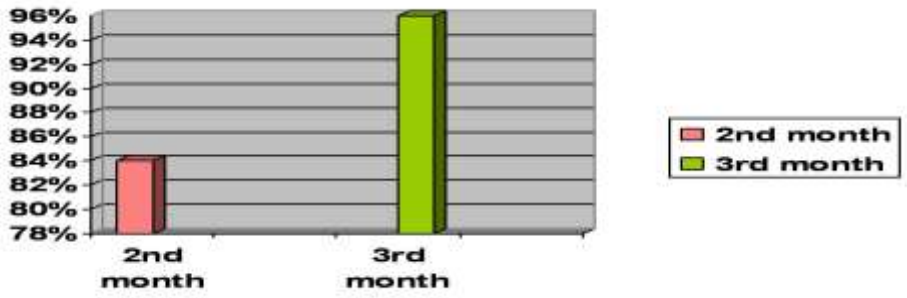
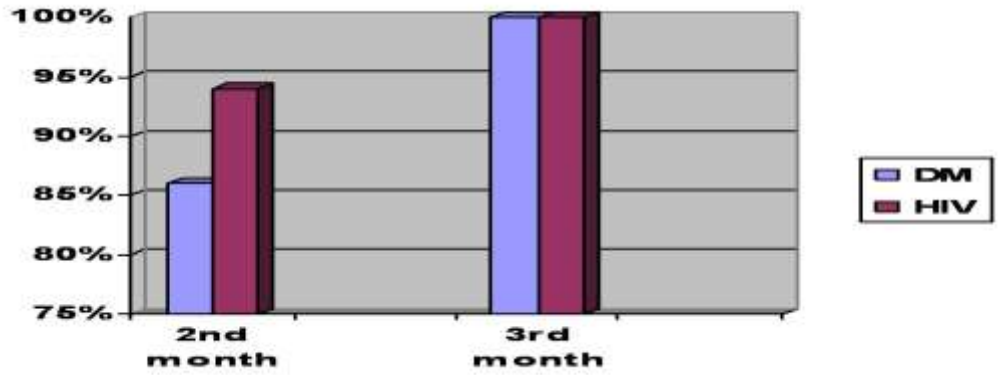


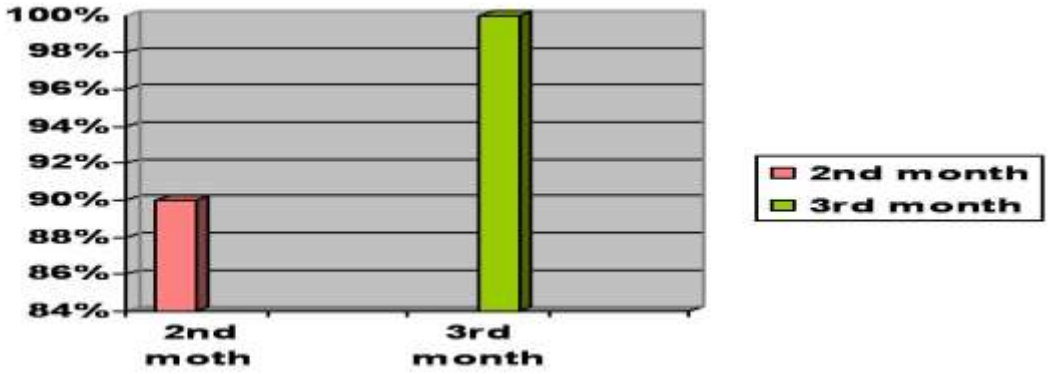
Fig. 3: Sputum conversion at the end of intensive phase

Immunocompetent group (a):



Immunocompromised group (b):





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