

TREATMENT ADHERENCE AND FACTORS INFLUENCING ADHERENCE OF DRUG SENSITIVE PULMONARY TUBERCULOSIS PATIENTS ON DAILY DRUG REGIMEN WITH FIXED DOSE COMBINATION: A CROSS-SECTIONAL STUDY AT DOTS CENTER IN RAJENDRA INSTITUTE OF MEDICAL SCIENCES, RANCHI

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Abstract

Background: In Jharkhand, a tribal dominant state, tuberculosis remain the leading cause of mortality and morbidity among the infectious diseases. There are hardly any studies done to assess the adherence of TB treatment after the initiation of daily regimen under NTEP. Hence, we formed our study to identify the factors influencing adherence of daily drug regimen in FDC which will assist the effective program management. **Materials and Methods:** A cross sectional study conducted at DOTS centre of Rajendra institute of medical sciences Ranchi. All drug sensitive pulmonary TB patients in the age group of 16-80 years who were enrolled in the DOTS centre between 12th April 2021 till 12th October 2021 were selected by consecutive sampling technique. A total of 355 patients were included in the study for outcome of which we found 15 patients got transferred out so, only the remaining 340 patients have been included in the analysis of adherence and factors influencing their adherence during the course of anti-TB treatment. The protocol of the study strictly followed the Strengthening the reporting of observational studies in epidemiology (STROBE) guidelines. Data were analysed using SPSS V.20.0 software, and multiple logistic regression analysis was done to determine the predictors of treatment adherence. **Results:** We found significant association of treatment adherence with urban residence, non-tribal ethnicity, married status, nuclear family type, non-vegetarian diet habits (for support protein), positive contact history of TB, positive history of COVID-19 infection, availability of drugs in every visit, comfort in taking daily drug with fewer side effects, family supervision in taking medication and follow up after treatment are found to be statistically significant. A higher odd of adherence is seen in married patients (AOR=0.784, p=0.000), patients from a nuclear family (AOR=0.912, p=0.003) and in patients undergoing sputum examinations on follow up (AOR=0.495, p=0.000). **Conclusion:** From this study we concluded that family-based counselling and supervision, more care and support from a nuclear family setup and follow up after treatment can improve the adherence of the treatment based on daily drug regimen in FDC.

INTRODUCTION

Even though there has been tuberculosis medication for decades, the disease is still difficult to eradicate. It still remains the leading cause of death from a single infectious agent worldwide and causing heavy impact on economic development ranking above HIV/AIDS.^[1] Fortunately, effective anti TB treatment reduces the infectivity by 90% within 48 hours.^[2,3] The lack of patient commitment to the therapy due to its complexity, tolerability, and lengthy duration ultimately led to our failure in the war against TB, even if it initially appeared that we were winning. These challenges in turn decrease the adherence and which in turn increases the mortality failure and relapse rate and drug resistance and eventually leading to increased duration and challenges in treatment forming the vicious cycle of tuberculosis.^[4-10] Ending the disease will only be possible when patient is adhered to the treatment.

All age groups, particularly the productive ones from 15 to 45 years old and mostly men as well as residents of urban slums, are affected by TB. To achieve cure against TB, patients need to take more than 90% of TB medications. As per WHO treatment default are patients who interrupt treatment for two or more months.¹⁰ In India's NTEP, incentives and enablers are improvised to promote compliance and also 99DOTS a low-cost approach for monitoring and improving TB medication adherence was introduced.^[11] Studies shows that, daily TB regimens with FDC is convenient for patients which leads to improved compliance and prevent drug resistance.^[12,13,14] So, our study aims to identify the factors influencing adherence of daily drug regimen in FDC. There are hardly any studies done to assess these domains after the initiation of daily regimen. Hence, we formed our study to assist the effective program management.

In social economic perspective, the multidrug resistant TB increases the cost of treatment to over 100 times.^[15] Studies shows that FDC based regimen were associated with fewer side effects and are more acceptable to patients. In the daily regimen mostly three to four tablets per day depending on the weight band of the patient, which not only increases the adherence by decreasing pills burden, but also minimizes dispensing and prescription errors, dosing errors, and patient negligence errors.^[16] There was no clear definition for adherence in the literature. Hence, in our study adherence was defined as patient taken more than 80 to 90% of treatment doses which is evaluated as PDC (Proportion of Days Covered) $\geq 80\%$.^[17]

MATERIALS AND METHODS

This is a cross sectional study conducted in Jharkhand a tribal dominant state, at DOTS center of Rajendra institute of medical sciences Ranchi. The

study includes all drug sensitive pulmonary TB patients in the age group of 16-80 years who have enrolled in the DOTS center between 12th April 2021 till 12th October 2021. Out of the 15 patients, 11 patients were transferred to private institutions and we couldn't trace the remaining 4 patients with their given details. Which includes all new sputum positive, CBNAAT/LPA confirmed cases and previously treated less than one month [Figure 1].

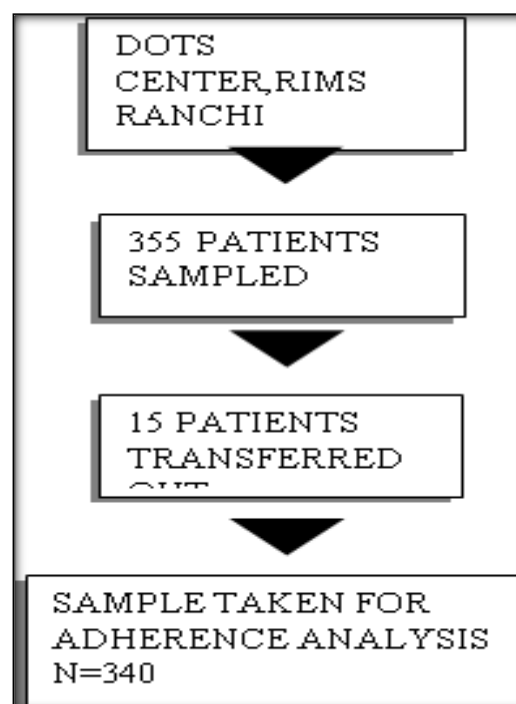


Figure 1: showing overall methodology of the study

Seriously ill patients, age less than 16 years, pregnant women, drug resistant TB, patients with physical and cognitive limitations including psychiatric illness are excluded from the study. Which gives the sample size of our study as 355. Data is collected using consecutive sampling technique. Data collection done using pre-tested, semi structured questionnaire by means of direct interview in DOTS center/residence of patient or over phone calls whichever the patient feels comfortable. The protocol of the study strictly followed the Strengthening the reporting of observational studies in epidemiology (STROBE) guidelines.

Data Analysis

Data management was done in Microsoft Excel V.2007 and statistical analysis in SPSS V.20.0. Mean and SD were used to express quantitative data, while proportions and percentages were used for qualitative data. Regression analysis was done to understand the predictors, and the association between variables was interpreted using OR.

Proper written approval from Institution Ethics Committee has been taken. The medical officer of DOTS center has been informed and permission was taken for the conduct of the study. Proper written

consent from patients have been obtained after acknowledging privacy and confidentiality.

RESULTS

Socio demographic profile of patients shows most of them belongs to economically productive age group of 16-30 years (42.9%), females (50.6%), Hindu

religion (62.1%), non-tribal ethnicity (60.9%), urban region (72.4%), married (81.5%), and having nuclear family (67.1%). There is statistically significant association with treatment adherence among, urban residence, non-tribal ethnicity, married status, and nuclear family type. Other sociodemographic determinants were found statistically non-significant as shown in [Table 1].

Table 1: Sociodemographic profile of patients and their association with adherence (n=340)

Socio-demographic variables	Levels	Total (n=340)	Adherent (n=308)	Non-adherent (n=32)	Chi-square test	p value
Age group	16-30	146 (42.9)	133 (43.2)	13 (40.6)	5.213	0.266
	31-45	119 (35)	104 (33.8)	15 (46.9)		
	46-60	57 (16.8)	54 (17.5)	3 (9.4)		
	61-75	14 (4.1)	14 (4.1)	0		
	≥ 76	4 (1.2)	3 (1)	1 (3.1)		
Gender	Male	168 (49.4)	153 (49.7)	15 (46.9)	0.091	0.763
	Female	172 (50.6)	155 (50.3)	17 (53.1)		
Religion	Hindu	211 (62.1)	195 (63.3)	16 (50)	3.994	0.262
	Muslim	16 (4.7)	14 (4.5)	2 (6.3)		
	Cristian	49 (14.4)	45 (14.6)	4 (12.5)		
	Other	64 (18.8)	54 (17.50)	10 (31.3)		
Ethnicity	Tribal	133 (39.1)	112 (36.4)	21 (65.6)	11.221	0.001*
	Non-tribal	207 (60.9)	196 (63.6)	11 (34.4)		
Caste	General	100 (29.4)	94 (30.4)	6 (18.8)	10.721	0.013*
	OBC	100 (29.4)	95 (30.4)	5 (15.6)		
	SC	7 (2.1)	7 (2.3)	0		
	ST	133 (39.1)	112 (36.4)	21 (65.6)		
Address/Residence	Urban	246 (72.4)	228 (74.7)	18 (56.3)	4.579	0.032*
	Rural	94 (27.6)	80 (26.3)	14 (43.8)		
Socio-economy status**	Upper Class	3 (0.9)	3 (1.0)	0	3.704	0.448
	Upper middle Class	19 (5.6)	19 (6.2)	0		
	Middle Class	51 (15.0)	48 (15.6)	3 (9.4)		
	Lower middle	117 (34.4)	104 (33.8)	13 (40.6)		
	Lower Class	150 (44.1)	134 (43.5)	16 (50)		
Marital Status	Married	277 (81.5)	253 (82.8)	22 (68.8)	12.129	0.007*
	Unmarried	47 (13.8)	43 (13.6)	5 (15.6)		
	Widow	6 (1.8)	5 (1.6)	1 (3.1)		
	Divorced	10 (2.9)	6 (1.9)	4 (12.5)		
Type of Family	Nuclear	228 (67.1)	216 (70.1)	12 (37.5)	13.972	0.000*
	Joint	112 (32.9)	92 (29.9)	20 (62.5)		

*Statistically significant

**Modified BG Prasad Scale (AICPI January 2022)

We found patients with non-vegetarian diet habits are having statistically significant adherence to the treatment [Table 2]. In health profile, patient with positive contact history of TB, and positive history of COVID-19 infection were having significant adherence towards TB treatment [Table 3]. The most common reason for not making regular missed calls by the patients were, unable to operate mobile phone (37%) followed by no personal mobile phone (27%) [Figure 2].

Table 2: Diet and addiction related variables and their association with adherence (n=340)

Diet and addiction related variables	Levels	Total N (%)	Adherence N (%)	Non-adherence N (%)	Chi square test	p value
Types of smoking	Cigarette	53 (15.6)	49 (15.9)	4 (12.5)	0.643	0.725
	Bidi	59 (17.4)	52 (16.9)	7 (21.9)		
	Non smoker	228 (67.1)	207 (67.2)	21 (65.6)		
How frequently you take alcohol?	Social	23 (6.8)	23 (7.5)	0	5.666	0.059
	Occasional	22 (6.5)	22 (7.1)	0		
	Daily	2 (0.6)	2 (0.6)	0		
	Non alcoholic	293 (86.2)	261 (84.7)	32 (100)		
Any history of illicit drug addiction	Yes	10 (2.9)	10 (3.2)	0	1.07	0.301
	No	330 (97.1)	298 (96.8)	32 (100)		
Number of meals per day	≤2	1 (0.3)	1 (0.3)	0	5.869	0.053
	3	260 (76.5)	30 (93.8)	230 (74.7)		
	>3	79 (23.2)	2 (6.3)	77 (25)		

Food preference	Vegetarian	108 (32.8)	92 (29.9)	16 (50)	5.419	0.020*
	Non-vegetarian	232 (68.2)	216 (70.1)	16 (50)		

*Statistically significant

Table 3: Health profile of total, adherent and non-adherent patients and their association with adherence (n=340)

Health profile variables	Levels	Total N (%)	Adherent N (%)	Non-adherent N (%)	Chi square test	p value
BCG Vaccination	Yes	253 (74.4)	231 (75)	22 (68.8)	0.595	0.441
	No	87 (25.6)	77 (25)	10 (31.2)		
Contact history of TB	Present	220 (64.7)	190 (61.7)	30(93.8)	13.048	0.000*
	Absent	120 (35.3)	118 (38.3)	2 (6.3)		
History of COVID-19 infection	Present	210 (61.8)	183 (59.4)	27 (84.4)	7.647	0.006*
	Absent	130 (38.2)	125 (40.6)	5 (15.6)		
History of prolonged medication	Yes	131 (38.5)	120 (39)	11 (34.4)	0.257	0.612
	No	209 (61.5)	188 (61)	21 (65.6)		

*Statistically significant

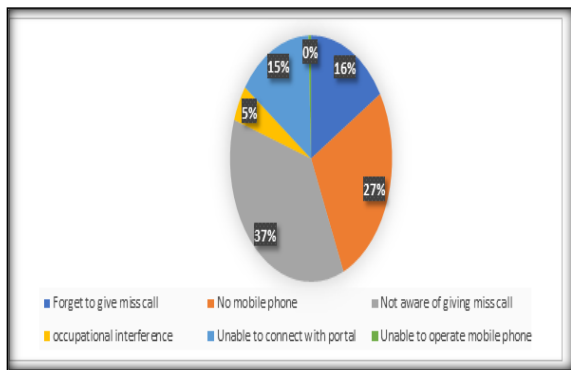


Figure 2: Reasons for not making regular missed calls (n=191)

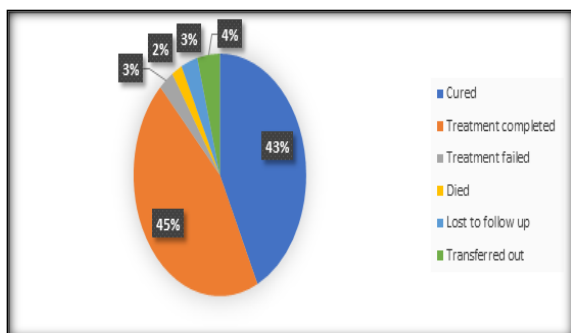
Statistically significant adherence was found with the availability of drugs in every visit (patient was not felt short of drug and got their drug regularly

even in lockdown during COVID-19 pandemic without any difficulties) and comfort in taking daily drug with fewer number of tablets. Supervision of medication play major role in adherence of treatment and follow up of the TB patient by sputum examination is also very important component in control of TB which we found statistically significant in our study Table 4. Out of 355 TB patient, 152 (43%) were cured, 160 (45%) were declared as treatment completed, 10 (3%) whose sputum smear or culture is found positive even at month five or later during treatment so called treatment failed group, 7 (2%) were died during course of treatment, about 11 (3%) were in lost to follow-up category and 15 (4%) were transferred out [Figure 3].

Table 4: Variables influencing the adherence and their association with adherence (n=340)

Variables	Levels	Total	Adherent	Non-adherent	Chi square test	p value
Average time of travel to get TB drug from home to DOTS center	<15min	28 (8.2)	28 (9.1)	0	5.617	0.060
	31-60min	221 (65)	202 (65.6)	19 (59.4)		
	>60min	91 (26.8)	78 (25.3)	13 (40.6)		
Distance of DOTS center from your home?	<6km	240 (70.6)	221 (71.8)	19 (59.4)	2.139	0.144
	>6km	100 (29.4)	87 (28.2)	13 (40.6)		
TB drugs available in every visit	Yes	336 (98.9)	307 (99.7)	29 (90.6)	20.422	0.000*
Feel inconvenience in taking medicine every day	No	4 (1.2)	3 (9.4)	1 (0.3)	51.568	0.000*
	Yes	14 (4.1)	5 (1.6)	9 (28.1)		
Family supervision in taking medication	No	326 (95.9)	303 (98.4)	23 (71.9)	18.639	0.000*
	Never	32 (9.4)	28 (9.1)	4 (12.5)		
	Sometime	81 (23.8)	64 (20.8)	17 (53.1)		
	Often	227 (66.8)	216 (70.1)	11 (34.4)		
Knowledge in how many months of treatment you can be cured	4 months	12 (3.5)	10 (3.2)	2 (6.3)	6.439	0.092
	6 months	268 (78.8)	248 (80.5)	20 (62.5)		
	8 months	47 (13.8)	40 (13)	7 (21.9)		
	10 months	13 (3.8)	10 (3.2)	3 (9.4)		
Knowledge of irregular anti-TB treatment can infect your other family members too	yes	298 (87.9)	271 (88)	27 (84.4)	0.349	0.555
	No	42 (12.4)	37 (12)	5 (15.6)		
Receive cash in your bank account	Yes	160 (47.1)	144 (46.8)	16 (50)	0.123	0.726
	No	180 (52.9)	164 (53.2)	16 (50)		
Tribal population receive Rs750/ single time as treatment started	Yes	123 (36.2)	107 (34.7)	16 (50)	3.180	0.204
	No	8 (2.4)	7 (2.3)	1 (3.1)		
	Not applicable	209 (61.5)	194 (63)	15 (46.9)		
Sputum examination after initiation of ATT for follow up	Yes	330 (97.1)	305 (99)	25 (78.1)	44.361	0.000*
	No	10 (2.9)	3 (1)	7 (21.9)		

*Statistically significant



*The outcomes have been calculated on 355, including 15 transferred out patients

Figure 3: Pie chart showing the outcomes of treatment (n=355*)

The results of multiple logistic regression shows that tribal ethnicity (AOR=1.104, p=0.002), vegetarian food preference (AOR=1.1, p=0.005) were associated with a significantly higher chance of non-adherence. Higher chances of non-adherence are also seen in patients living among patients with

history of contact with tuberculosis (AOR=1.026, p=0.639, NO/ occasional history of family supervision (AOR=1.070, p=0.150) and (AOR=1.049, p=0.159), although the differences were not statistically significant.

Significantly lower odds of non-adherence were seen in married patients (AOR=0.784, p=0.000), patients from a nuclear family (AOR=0.912, p=0.003) and in patients undergoing sputum examinations on follow up (AOR=0.495, p=0.000). In widows (AOR=0.883, p=0.337), patients with history of COVID-19 infection (AOR=0.976, p=0.626) and patients getting TB drugs regularly (AOR=0.957, p=0.737) from the DOTS center, the odds of non-adherence were lower although not statistically significant. No significant change was seen in terms of increasing age in non-adherence among the study cohort [Table 5].

Table 5: Table showing the results of multiple logistic regression (n=340)

Variables	Levels	Adjusted Odds ratio	Sig.
Ethnicity	Tribal	1.104	.002*
	Non-tribal	1 (Reference)	
Marital status	Married	.784	.002*
	Widow	.883	.337
	Divorced	.1.064	.426
	Unmarried	1 (Reference)	
Type of family	Nuclear	.912	.003*
	Joint	1 (Reference)	
Food preference	Vegetarian	1.100	.005*
	Non-vegetarian	1 (Reference)	
Contact with tuberculosis	Yes	1.026	.639
	No	1 (Reference)	
H/O of COVID-19 infection	Yes	.976	.626
	No	1 (Reference)	
Get TB drugs regularly	Yes	.957	.737
	No	1 (Reference)	
Family supervision	Never	1.070	.150
	Occasional	1.049	.159
	Often	1 (Reference)	
Sputum examination on follow up	Yes	.495	0.000*
	No	1 (Reference)	
Age		.999	.397

*Statistically significant

DISCUSSION

Most studies in India and abroad were focused on treatment adherence of TB patients on intermittent therapy. Studies on daily TB regimen are either older or based on individual Anti-TB medication grouped together. Daily medication schedule with FDC under NTEP and monitoring using 99DOTS is reported to promote patient adherence. Despite that our present study, shows a non-adherence of 9.4% among patients. Similar 22% non-adherence was also noted in research by Motappa et al, in Mangalore City.^[18]

The majority of patients in our current study (43.4%) are in the 16-30 age group, which is the economically most productive age group, and are

females (50.1%), which is consistent with the study conducted by Kaur et al.^[19] In a study by Kolappan et al in Tiruvallur district of Tamilnadu also found that majority 47.4% were from 15-34 years age group and more females than males (51.2% vs 48.8%).^[20] The majority of the people in our study (39.1%) belonged to a Scheduled Tribe and according to the modified BG Prasad SES (2022), almost half (44.2%) belongs to lower class. This is consistent with research conducted by Trivedi et al. in a comparable location of Rewa, Madhya Pradesh, with ST patients (30.8%), and 3/4 of the patient population is from a lower socioeconomic status.^[21]

In our study family members or spouse consistently encouraged patients to take their medications and eat nutrient diet. This is in line with literature and a recent study done in Armenia suggesting family-

based TB counselling significantly improves treatment adherence through interpersonal relationship.^[22,23] Our study found significant adherence in patients from joint family and married patients. Comparison of adherent and non-adherent patient shows no significant difference between age group, gender, religion, ethnicity, caste, and socio-economic scale.

In our study more than half of the study participants were not calling toll free number regularly due to multiple reasons. This is similar to report given by Thomas BE et al stating India's 99DOTS had high acceptance among Health Care Professionals but variable acceptance among patients.^[24] Some are modifiable but others such as poor cell phone accessibility, cellular signal, literacy are more difficult to address. In a study conducted by Krasniqi et al, awareness about long duration of treatment, risk of spread to family members, and adverse events play an important role in treatment adherence.^[25] In our study we found no significant difference about these factors which is in concordance with the study done by Das et al.^[26] In our study 36.1% had difficulty in accessing treatment due to travel expenses followed by 27.7% patients due to financial issues which is in line with the recent qualitative review stating economic constraints of direct and indirect causes of accessing treatment. Hence there is a need to improve incentives and enablers as shown by literature.^[27] Alcoholism interferes with efficacy of drugs and hampers the regularity of regimen. In our study, smoking and alcohol consumption pose significant challenges for healthcare workers in line with other studies (1.5-2.9%). This demonstrates the need for psychiatric and dead diction counselling to be included under NTEP and also suggests against smoking and alcohol abuse, laws and regulations must be strengthened.^[28]

CONCLUSION

From this study it can be concluded that, the area where the patient resides, their ethnicity, their marital status, type of house and family they belong, total number of persons and rooms available in their house, non-vegetarian diet, contact history of TB patient and history of covid 19 infection, availability of TB drugs in every visit, lesser side effects from the drugs, lesser number of tablets, supervision of medication and follow up of TB patients are found statistically significant for adherence towards TB management. Other socio-demographic determinants, long history of taking medication for other illness, BCG vaccination was found non significance towards adherence of treatment. From this we can understand that family-based counselling and supervision, care from a nuclear family setup and follow up after treatment can improve the adherence of the treatment based on daily drug regimen in FDC.

The lack of universal definition of adherence makes comparison with other studies difficult. Though the study has sufficient sample size, the study setting and location makes the results non-generalizable for pan India assumptions. Adherence to TB medication in multifactorial, so a single factor cause effect relationship could not established. The study only included drug sensitive TB cases and hence not representative for other forms of TB like drug resistant TB. A detailed study which includes drug resistant TB patients can pave a way for better comprehension.

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Competing interests None.

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