Outcome Analysis of Pulmonary Tuberculosis Patients on Daily Drug Regimen with Fixed Dose Combination during COVID-19 Pandemic: A Cross Sectional Study at Rajendra Institute of Medical Sciences, Ranchi

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Abstract

Background: In the tribal predominant state of Jharkhand, daily drug regimen in FDC was introduced during 2015-16. There are not many studies done to assess the outcome of TB treatment after the initiation of daily regimen under NTEP. Hence, we formed our study to identify the socio-demographic profile and factors influencing outcome of daily drug regimen in FDC which will provide the scientific intuition on tuberculosis management.

Design: A cross sectional study was conducted at DOTS center 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 center between 12th April 2021 till 12th October 2021 were selected by consecutive sampling technique and followed up for 9 months. A total of 355 patients were included in the study for outcome and socio demographic profile 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 analyzed using SPSS V.20.0 software,

Results: Patients having urban residence (12.398, p<0.001), nuclear family type (15.543, p<0.001), less than four persons in the family (16.728, p<0.001), less than two rooms in house (15.597, p<0.001), DOTS center distance less than 6km (9.943, p<0.002), drug availability on daily visit(10.925, p<0.001), Follow up with sputum examination (130.72, p<0.001) and follow up visit by Health care workers (107.52, p<0.001), Daily taking the drug (67.001, p<0.001) and knowledge of treatment duration (5.844, p=0.02), have significant association with better treatment outcome. Taking alcohol daily(37.492, p<0.001), Forgot taking pills (136.08, p<0.001), stopped without informing treatment provider (144.88, p<0.001), Stopped drug when feeling good

(153.03, p<0.001), Inconvenience in taking daily (20.483, p<0.001) and Not receiving initial 750rs by tribal people (26.331, p<0.001)are having significant association with undesired treatment outcome during TB management.

Conclusions: From this study, we can understand that, knowledge about the disease and treatment, easy accessibility and availability of the drug, motivations like incentives and follow up of the patients, deaddiction from alcohol, reminders calls, adherence counselling and drugs with lesser side effects will pave the way for better results while managing tuberculosis using the current regimen.

Keywords: Drug Sensitive Tuberculosis, Fixed Dose Combination, Outcome, NTEP, DOTS, Daily Regimen.

Introduction

Tuberculosis, anancient killer disease, still persists as the leading cause of ill health and death worldwide and causing devastating damage to countries in health and economy aspects. Widely, there are two types of tuberculosis that are pulmonary and extra-pulmonary. The former affects the lungs and latter affects all other tissues in the body. Though man has no inherited immunity against tuberculosis, tuberculosis is preventable and curable [1,2].

Our study was conducted amidst covid 19 pandemic (2021-22), when the health system undergone an obvious negative impact in providing public health services. So that, we can have an overall idea of how service provisions get affected during a dire situation and to provide recommendations on effective steps to be taken to lower the effect of future emergencies on service provision. The most obvious effect is a global drop in newly diagnosed and reported tuberculosis cases of 1.3 million (7.1 million in 2019 to 5.8 million in 2020) of which 41% drop is contributed by India [3]. TB costs us 1.3 million lives globally, of which nearly 5 lakhs people are from India [4].

Not to forgot the ill-effect of pandemic on global spending on TB diagnosis, treatment, and prevention services dropped to 5.3 billion in 2020, which is less than half of what is needed [3]. Though the anti-TB programmes in India are revised and upgraded, we are still struggling to tackle the barriers in completing TB treatment and reaching desired outcome. These barriers in reaching a desired outcome are multidimensional including socio-demographic, knowledge, attitude, behavior, economy...etc.

In Jharkhand, daily drug regimen replaced the intermittent regimen in FDC during 2015-16. There are not many studies done to assess the outcome of TB treatment after the initiation of daily regimen under NTEP. Therefore, this study was aimed to evaluate the outcome of daily drug regimen in fixed dose combination among drug sensitive tuberculosis patients registered at DOTS center in Ranchi. With that in mind, we devised our objectives to describe the socio-demographic distribution and evaluation of outcome of daily drug regimen in FDC among drug sensitive tuberculosis patients registered at DOTS center in Ranchi. As per intention to treat analysis, in our study, we considered patients who were cured or treatment completed as good outcomes and all other outcomes like treatment failed, died, lost to follow-up and transferred out patients as bad outcomes.

Methodology

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 and patients are follower for a period of 9 months. Which includes all new sputum positive, CBNAAT/LPA confirmed cases and previously treated less than one month.

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. Out of these 355, 15 patients were transferred out. Out of the 15 transferred out patients, 11 patients were transferred to private institutions and we couldn't trace the remaining 4 patients with their given details 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.

Table **1**)

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. Bivariate analysis using chi-square test to determine association with outcome of treatment.

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 of the participants.

Results

Most of the patients belongs to the age group of 16-45 years (77.9%). Most of them are males (49.4%) and belonging to Hindu religion (62.1%). Majority of them belongs to non-Tribal ethnicity (60.9%) and scheduled tribe caste (39.1%). Most of them belongs to urban residence (72.4%) and lower class in socio economic scale (44.1%). Most of them are married (81.5%) and belong to nuclear family type (67.1%). ()

Table 1: Socio-demographic profile of the patients

Socio-demographic variables	Levels	Total(n=340)
Age group	16-45 years	265 (77,9%)
	>45 years	75(22.1%)
Gender	Male	168 (49.4)
	Female	172 (50.6)
Religion	Hindu	211 (62.1)
	Muslim	16 (4.7)
	Cristian	49 (14.4)
	Other	64 (18.8)
Ethnicity	Tribal	133 (39.1)
	Non-tribal	207 (60.9)
	General	100 (29.4)
	OBC	100 (29.4)

Caste	SC	7 (2.1)
	ST	133 (39.1)
Address/Residence	Urban	246 (72.4)
	Rural	94 (27.6)
Socio-economy status**	Upper Class	3 (0.9)
	Upper middle Class	19 (5.6)
	Middle Class	51 (15.0)
	Lower middle	117 (34.4)
	Lower Class	150 (44.1)
Marital Status	Married	277 (81.5)
	Unmarried	47 (13.8)
	Widow	6 (1.8)
	Divorced	10 (2.9)
Type of Family	Nuclear	228 (67.1)
	Joint	112 (32.9)

Age, gender, ethnicity, caste, marital status, family income and socio-economic status are not having significant association with the outcome variable. Hindu religion (20.073, p<0.001), urban residence (12.398, p<0.001), Nuclear family type (15.543, p<0.001), less than four persons in the family (16.728, p<0.001), less than two rooms in house (15.597, p<0.001) are having significant association with better outcome from treatment. (Table 2) Taking alcohol daily have a significant association with bad outcomes for the tuberculosis treatment (37.492, p<0.001). other variables belonging to personal habits and personal preference category, are not having significant association with the outcome. (Table 3) DOTS center distance less than 6 km (9.943, p<0.002), drug availability on daily visit (10.925, p<0.001), follow up with sputum examination (130.72, p<0.001) and follow up visit by Health care workers (107.52, p<0.001) were having significant association with good outcome from treatment. Not receiving 750rs was significantly associated with bad outcome for tribal people (26.331, p<0.001). Other variables like time to reach DOTS center, family supervision and other incentives are not having significant association with the treatment outcome (Table 4). Taking the drug daily (67.001, p<0.001) and knowledge of treatment duration (5.844, p=0.02). having significant association with better treatment outcome. Forgot taking pills (136.08, p<0.001), stopped without informing treatment provider (144.88, p<0.001), Stopped drug when feeling good (153.03, p<0.001), Inconvenience in taking daily (20.483, p<0.001) are having significant association with undesired treatment outcome during TB management. (Table 5)

Table 2: Association of socio demographic details with treatment outcome

Variables	Class	Bad Outcome [B]		Good Outcome [A]		Chi²	P-
		n	%	n	%	Value	Value
Age	16-45years	34	79.1%	243	77.9%	0.031	0.860
	>45 years	9	20.9%	69	22.1%		
Gender	Males	24	55.8%	153	49.0%	0.694	0.405
	Females	19	44.2%	159	51.0%		
Religion	Hindu	16	37.2%	204	65.4%	20.073	<0.001*
	Muslim	6	14.0%	11	3.5%		
	Christian	6	14.0%	45	14.4%		
	Others	15	34.9%	52	16.7%		

Ethnicity	Tribal	21	48.8%	114	36.5%	2.426	.119
	Non-Tribal	22	51.2%	198	63.5%		
Caste	General	11	25.6%	92	29.5%	4,759	0.190
	OBC	8	18.6%	97	31.1%		
	SC	1	2.3%	7	2.2%		
	ST	23	53.5%	116	37.2%		
Residence	Urban	21	48.8%	233	74.7%	12.398	<0.001*
	Rural	22	51.2%	79	25.3%		
Marital Status	Married	30	69.8%	257	82.4%	6.809	0.078
	Unmarried	8	18.6%	44	14.1%		
	Divorced	2	4.7%	4	1.3%		
	Widow	3	7.0%	7	2.2%		
Family Type	Nuclear	17	39.5%	218	69.9%	15.543	<0.001*
	Joint	26	60.5%	94	30.1%		
No Of Persons In The Family	<=4 persons	15	34.9%	209	67.0%	16.728	<0.001*
	>4 persons	28	65.1%	103	33.0%		
No Of Rooms In House	Up to 2 Rooms	15	34.9%	206	66.0%	15.597	<0.001*
	More than 2 Rooms	28	65.1%	106	34.0%		
Family Income	Up to 5000rs/month	22	51.2%	198	63.5%	2.426	0.119
	More than 5000rs/month	21	48.8%	114	36.5%		
Ses	Class 4 & 5	35	81.4%	241	77.2%	.377	.539
	Up to class 3	8	18.6%	71	22.8%		

*Statistically significant.

Table 3: association of personal habits and preference variables with treatment outcome

Variables	Class	Bad Outcome B		Good Outcome A		Chi²	P-
		N	%	N	%	Value	Value
Smoking Habit	Yes	13	30.2%	103	33.0%	0.133	0.716
	No	30	69.8%	209	67.0%		
Alcohol Habit	Yes	6	14.0%	46	14.7%	0.019	0.891
	No	37	86.0%	266	85.3%		
Alcohol Habit Frequency	Social	2	4.7%	23	7.4%	37.492	<0.001*
	Occasional	1	2.3%	22	7.1%		
	Daily	6	14.0%	1	0.3%		
	Non-Alcoholic	34	79.1%	266	85.3%		
Alcohol Duration	<=5 Years	3	7.0%	35	11.2%	3.630	0.163
	>5 Years	4	9.3%	11	3.5%		
	Non-Alcoholic	36	83.7%	266	85.3%		
No. Of Meals/Day	<=2 Times	1	2.3%	1	0.3%	4.818	0.090
	3 Times	36	83.7%	235	75.3%		
	>3 Times	6	14.0%	76	24.4%		
Food Preference	Vegetarian	12	27.9%	99	31.7%	0.257	0.612
	Non Vegetarian	31	72.1%	213	68.3%		

BCG Vaccination	Yes	29	67.4%	235	75.3%	1.231	0.267
	No	14	32.6%	77	24.7%		
Contact H/O Tb	Yes	30	69.8%	194	62.2%	0.935	0.334
	No	13	30.2%	118	37.8%		
H/O Covid-19	Yes	30	69.8%	188	60.3%	1.443	.230
	No	13	30.2%	124	39.7%		

*Statistically significant.

Table 4: service-related variables and their association with treatment outcome

Variables	Class	Bad Outcome [B]		Good Outcome [A]		Chi^2	P-
		N	%	N	%	Value	Value
Travel Time To Dots	<=15mins	1	2.3%	27	8.7%	2.083	0.149
	>15mins	42	97.7%	285	91.3%		
Dots Distance	<6km	21	48.8%	226	72.4%	9.943	<0.002*
	>6km	22	51.2%	86	27.6%		
Drug Availability	Yes	40	93.0%	310	99.4%	10.925	<0.001*
	No	3	7.0%	2	0.6%		
Family Supervision	Yes	3	7.0%	30	9.6%	0.312	0.576
	No	40	93.0%	282	90.4%		
Amount Received In Account	Yes	15	34.9%	145	46.5%	2.051	0.152
	No	28	65.1%	167	53.5%		
750rs Once For Tribals	Yes	16	37.2%	107	34.3%	26.331	<0.001*
	No	8	18.6%	7	2.2%		
	NA	19	44.2%	198	63.5%		
Sputum Follow Up	Yes	24	55.8%	310	99.4%	130.72	<0.001*
	No	8	18.6%	2	0.6%		
	NA	11	25.6%	0	0.0%		
Health Worker Visit	Yes	16	37.2%	267	85.6%	107.52	<0.001*
	No	15	34.9%	45	14.4%		
	NA	12	27.9%	0	0.0%		

*Statistically significant.

Table 5: Association of knowledge and attitude-based variables with outcome

Variables	Class	Bad Outcome [B]		Good Outcome [A]		Chi^2 Value	P-Value
Regularity In Taking Drug	Yes	34	79.1%	312	100.0%	67.001	<0.001*
	No	9	20.9%	0	0.0%		
Give Miss Calls	Yes	18	41.9%	141	45.2%	0.170	0.680
	No	25	58.1%	171	54.8%		
Forgot To Take Pills	Yes	24	55.8%	7	2.2%	136.08	<0.001*
	No	19	44.2%	305	97.8%		
Stopped Without Informing Provider	Yes	20	46.5%	1	0.3%	144.88	<0.001*
	No	23	53.5%	311	99.7%		
Stopped Drug When Feeling Good	Yes	21	48.8%	1	0.3%	153.03	<0.001*
	No	22	51.2%	311	99.7%		
	Yes	8	18.6%	9	2.9%	20.483	<0.001*

Inconvenience In Taking Daily	No	35	81.4%	303	97.1%		
Knowledge Of Treatment Duration	Yes	28	65.1%	253	81.1%	5.844	0.02*
	No	15	34.9%	59	18.9%		
Knowledge About Family Spread	Yes	38	88.4%	275	88.1%	0.002	0.965
	No	5	11.6%	37	11.9%		

*Statistically significant.

Discussion

The significant association of urban residence and Hindu religion can be explained by the increased accessibility of the health services by these cohorts compared to others. As per literature joint family, increased house space and increased number of rooms are suggested to decrease the spread of TB infection which might not be the case in terms of treatment outcome, seen from the results of the current study. Daily regimen followed by NTEP consists of FDC and monitoring through 99-DOTS which are reported to produce a better outcome than the older intermittent regimen. Our study is mostly composed of patients belonging to 16-45 years age group (77.9%) who are economically more productive than the others. Which is in concordance with a study done by Bisoi *et al*, reporting maximum patients belongs to the similar 15-54 years age group (79.1%) [5].

In our present study majority of the study population were scheduled tribes (39.1%) which is similar to study conducted by Goel *et al*, reporting higher SC/ST population (32.7%) [6]. Same study reporting the majority participants belonging to lower socio-economic status among their study cohort which is concordance with our current study having almost half (44.1%) of the included cohort belonging to the lower class according to modified BG prasad scale (AICPI January 2022) [6]. In a retrospective study conducted by Bhangari *et al* reported 54.5% of the patients on daily regimen were cured which is similar to our current study with 43% of cured participants [7].

A study done by Das *et al* reported that basic knowledge of TB treatment duration has no significant difference among adherence and better outcome which is in discordant with our current study stating knowledge about the duration of TB treatment produces better outcomes in more than 80% of the study participants [8]. The literature shows that offering money and transportation stipends to TB patients helps in clinical improvement especially for people who are in more vulnerable situations, which corroborates with the findings of our current study [9,10].

Alcoholism interferes with efficacy of drugs, regularity of treatment and thereby leads to undesired outcome which is in concordance with our study reporting significant association between frequency of taking alcohol and undesired outcome [11]. Hence regulations for controlling alcohol addiction and accessibility of deaddiction centers becomes crucial for better outcome from treatment.

Conclusion

We can conclude from the study that belonging to Hindu religion, urban residence, nuclear family, less than four persons in the family, less than two rooms in the house, distance of DOTS center less than six kilometers from the patients residence, availability of drug during each visit, incentives for tribal patients, sputum follow up after ATT, follow up by health care worker, regularity in taking the drug daily, knowledge about the treatment duration have significant association with better outcome of

tuberculosis treatment. Daily frequency of alcohol consumption, forgetting to take pills, stopping the drug without providers knowledge and inconvenience while taking drug are having significant association with unfavorable outcomes. From this study, we can understand that, knowledge about the disease and treatment, easy accessibility and availability of the drug, motivations like incentives and follow up of the patients, deaddiction from alcohol, reminders calls, adherence counselling and drugs with lesser side effects will pave the way for better results in tuberculosis management.

Despite having a significant sample size, the study's location and environment prevent the conclusions from being generalizable to India as a whole. A single component cause and effect link could not be identified due to the multivariate nature. 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 might lead to a clearer understanding.

Ethics approval: This research was approved by the Institutional Ethics Committee, RIMS, Ranchi, Jharkhand, India.

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