

A Systemic Analysis On Response To DOTS Regimen On Opportunistic HIV Infected Patient With Tuberculosis In A Tertiary Care Hospital; A Clinical Pharmacist Perspective To Enhance Healthcare

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Abstract

Background: Opportunistic infections are ailments and pathologies that occur more commonly and radically severely in patients exposed to the human immunodeficiency virus (HIV) due to the impaired and suppressed immune systems. Tuberculosis is the most common devious opportunistic infection occurring among HIV-positive patients in India. Various global tuberculosis treatment guidelines clearly endorse utilizing an individual patient-centered case management approach by directly observed therapy ("DOT").

Methodology: A Retrospective and Cross-Sectional study were carried out in the Revised National Tuberculosis Control Programme (RNTCP) Centre at Erode Government Hospital. Patient samples of HIV co-infected with TB were 52 and the study duration was 6 months. The objectives of the current study were to assess the patient's adherence to treatment by using MGL questionnaire, evaluate the treatment response, and monitor CD4 lymphocyte count in a tertiary care hospital. The results were analyzed by using SPSS software.

Results: Regarding the demographic details of the patients, 52 patients were examined, 31(59.6%) were male and 21(40.39%) were females. Comparing the treatment response, at the initiation and at the end of the treatment regime, the signs and symptoms were significantly reduced in patients, only 12 patients showed fatigue and 6 patients showed the symptom of weight loss. The High adherence of the patients improved from 9.61% to 65%. There is a statically significant ($p = 0.087$) results for CD4 count during ATT treatment.

Conclusion: Regular monitoring of patients' adherence is inevitable to enhance their response to the DOTS regimen and at the final stage can improve the patient's quality of life.

Keywords: Opportunistic infections, Tuberculosis, CD4 lymphocyte count, Healthcare, Human Immunodeficiency Virus (HIV)

INTRODUCTION:

One of the most common opportunistic infections in people is tuberculosis (TB) who have Acquired Immunodeficiency Syndrome (AIDS) /Human Immunodeficiency virus (HIV) [1]. TB and HIV are often called a dual epidemic. Worldwide, HIV infection contributed to 0.76 million incident TB cases, and HIV positive individuals were predicted to have died from TB at a rate of 208,000 in 2019 [2]. Mycobacterium tuberculosis and HIV amplify one another in the individual host, exacerbating the degradation of immune capabilities and, if left untreated, leading to early mortality [3]. People living with HIV are around 30 times more likely to develop TB than HIV negative people [4]. This is a result of PLHIV having decreased and inadequate innate and passive immunity to TB, [5] increasing the likelihood of developing a new case of TB infection [6] as well as transforming a latent infection into an active one. Monitoring patients' CD4 counts makes it easiest to determine the degree of immunosuppression, which decreases as PLHIV TB risk prevalence rises. Therefore, the primary indicator of immunological failure in

the development of HIV illness is the CD4 cell count. The commencement of ART therapy is described as the assessment of CD4-T cell count. When starting therapy for opportunistic infections like Tuberculosis and monitoring CD4 T cell count for ART effectiveness [7]The various factors increase the risk of TB in PLHIV are A very low level of CD4 count (<50 cells/ μ l) [8], restricted physical activity, Loss of appetite, weight loss, Anemia, Cigarette Smoking, Economic Status, literacy rate, Non-Compliance to the medications, Households, Inappropriate preventive measures(vaccinations) [9]. Patient Adherence to Anti-TB therapy is essential to achieve positive outcomes for both patients and community. Pharmaceutical care in Anti-Tubercular and Anti-Retroviral therapy is more important to get an adequate outcome in treatment. This study helps in analysis of treatment response and prescribing pattern of drugs for patients with HIV and TB.

Patients and Methods:

Study Design and Study Setting:

This Retrospective and Cross-Sectional study was carried out in Revised National Tuberculosis Control Programme (RNTCP) Centre at Erode Government Hospital. Patients samples of HIV co-infected with TB were 52 and the study duration was 6 months from January 2022-June 2022. In this study we included HIV with TB patients and excluded the patients with other comorbidities, pregnant and lactating women and the patients only with TB. Well-structured data collection forms were used to gather sociodemographic information, clinical and medication histories, laboratory test results, regular ward rounds, prescriptions monitoring, and medical professionals' reports. The study was approved by Institutional Ethics Committee of Dhnavantri Multispecialty Hospital, Erode (REF: DCC/IEC/025/2021).

The socio-economic status of patients was collected by using Kuppuswamy Socio Economic Scale. Depends upon the history of prior ATT and the findings from the recent sputum results, anti-tubercular managements were initiated for the suspected individuals. There were three different regimens used: Cat I: 2H3R3E3Z3/4H3R3, Cat II: 2S3H3R3E3Z3/ 1H3R3E3Z3/5H3R3E3, and Cat III: 2H3R3Z3/ 4H3R3. Treatment response of patients to anti-tubercular drug was analyzed in 3 different period of time that is at starting, middle and end of the treatment and variation in CD4 cell count was analyzed in the patients under ATT and ART. Patient adherence to the medication was analyzed by using Morisky, Green, and Levine Medication Adherence Questionnaire. It consists of 4 questions and each one is scored "0" for yes,"1" for No response. The scores of "0" denotes High adherence,"1 or 2" denotes Medium Adherence and "3 or 4" represents Low Adherence. Pharmaceutical care was given by patient counseling program to improve patient's medication adherence. Provide information to the patients regarding disease, medication, diet, and life style modification and assisted the patients in clarifying the doubts and in taking suitable decisions with respect to the management of disease. A Patient satisfaction questionnaire was handed over to the patients to whom we counseled earlier to examine our impact, as clinical pharmacists, in patient education program on their condition and medication taking behavior.

Statistical Analysis:

In this study Chi square and Wilcoxon T tests were used to evaluate patient's response to under ART and ATT treatment by using SPSS version 20.0.

RESULTS:

Of 52 patients examined 31(59.6%) were male and 21(40.39%) were females. 24 (46.15%) of the patients were in age between 21-40 years and 23(44.23%) were between 41-60 years old. Only 2 (3.92%) patients were greater than 60 years old and 3 (5.7%)were below 20 years old.

In social status of patients, it was found that 20(38.46%) patients were smokers and 23(44.23%) were alcoholic. Among the patients 15(28.84%) had the habit of tobacco chewing.

According to the educational Status, the current study observed that most of the patients were illiterate 16 (34.64%) followed by 9(17.30) had primary school, and 3 (5.76%) had professional Education.

In the occupational status, most of the patients 12 (23.07%) were unskilled workers and 14 (26.92%) were on clerical and shop owners in the present study Kuppusamy Socio economic status revealed that 21 (40.38%) belongs to lower class (V) and followed by 13 (25%) were upper lower class (IV). Distribution of patient according to their demographic details is listed in Table1:

Table 1: Distribution of patient demographic details (n=52)

BACKGROUND CHARACTERISTIC	NUMBER	PERCENTAGE
AGE (YEARS):		
▪ 0-20	3	5.7%
▪ 21-40	24	46.15%
▪ 41-60	23	44.23%
▪ > 60	2	3.92%
SEX:		
▪ Male	31	59.61%
▪ Female	21	40.39%
CIGARETTE SMOKING:		
▪ Smoker	20	38.46%
▪ Non-Smoker	32	61.84%
ALCOHOLISM:		
▪ Alcoholic	23	44.23%
▪ Non-Alcoholic	29	55.77%
TOBACCO CHEWING:		
▪ Tobacco User	15	28.84%
▪ Tobacco Non-User	37	71.16%
EDUCATION STATUS OF PATIENTS:		
▪ Profession	3	5.76%
▪ UG/PG	5	9.61%
▪ Post High School	7	13.46%
▪ High School	8	15.38%
▪ Middle School	4	7.69%
▪ Primary School	9	17.30%
▪ Illiterate	16	34.64%
OCCUPATION STATUS OF PATIENTS:		
▪ Profession	3	5.76%
▪ Semi – Profession	7	13.46%
▪ Clerical, Shop Owner	14	26.92%
▪ Skilled Workers	5	9.61%
▪ Semi-Skilled Worker	7	13.46%
▪ Unskilled Worker	12	23.07%
▪ Unemployed	4	11.57% f
KUPPUSAMY SOCIO ECONOMIC STATUS:		
▪ Upper (I)	3	5.76%
▪ Upper Middle (II)	5	9.63%
▪ Lower Middle (III)	10	19.23%
▪ Upper Lower (IV)	13	25.00%
▪ Lower (V)	21	40.38%

In the current research, change in the Observation of signs and symptoms of Tuberculosis such as cough, weight loss, fever, dyspnea, chest pain, hemoptysis and fatigue in respondents in three different intervals, that is in initiation, middle and end of the ATT treatment were analyzed. At the initiation of the treatment almost all these symptoms were observed in Tuberculosis with HIV co-infected patients. Out of 52 patients, 51 (98.75%) were suffering from cough, 14 (78.84%) Weight loss, 47(90.38%) fever, 23 (44.23%) dyspnea, 48(92.30%) Chest pain and 50(96.15%) fatigue. Among the subjects, 8 (15.38%) patients were affected with hemoptysis. In the middle of DOTS treatment, the numbers of patients suffering from fatigue were reduced to 19(36.53) and cough reduced to 13(25%). Around 17(32.69%) patients showed weight loss but none of them presented with signs of hemoptysis.

At the end of the treatment, it was found 12 (23.07%) patients showed fatigue and 6(11.54%) patients showed the symptom of weight loss. Signs and Symptoms observed in initiation, middle and end of the treatment were represented in Table 2.

Table 2: Distribution of Clinical Signs and Symptoms in response to DOTS Treatments (n=52)

Clinical Parameters	Initiation of Treatment	Middle of Treatment	End of Treatment
Cough	51(98.07%)	13(25%)	1 (1.92%)
Weight Loss	41(78.84%)	17 (32.69%)	6 (11.54%)
Fever	47(90.38%)	5(9.61%)	0
Dyspnea	23(44.23%)	1(1.92%)	0
Chest Pain	48 (92.30%)	5(9.61%)	1 (1.92%)
Hemoptysis	08 (15.38%)	1(1.92%)	0
Fatigue	50 (96.15%)	19 (36.53%)	12 (23.07%)

Table 3: Patients Showing Medication Adherence before and after Clinical Pharmacist Intervention (n=52)

Level of Adherence	Before Intervention	First Review	Second Review
Low	24 (46.15%)	13 (25.00%)	5 (9.61%)
Medium	19 (36.53%)	24 (46.15%)	13 (25.00%)
High	9 (17.03%)	15 (28.84%)	34 (65.38%)

In this study it has shown that during the ATT treatment, before clinical pharmacist intervention shown 24 (46.15%) low adherence and 9 (17.03%). In the second review, after Clinical pharmacist counselling, it was found that 5 (9.61%) low level of adherence and 34 (65.38%) higher adherence towards therapeutic management given in Table.3

Adherence of Patients According to Age Group

In the age group 0-20, about 3 (5.7%) of total 52 patients have treated for TB and out of these, 2 (3.92%) patients shown high adherence and 1(1.92%) shown medium adherence. In the age group 21-40, Among 24(46.1%) patients 17(70.83%) shown high adherence, 7 (29.17%) patients shown medium adherence and 1 (4.16%)patient shown low adherence and in the age group 41-60, 23 (44.23%) out of which 3(13.04%) patients shown low adherence to treatment and 2 (3.92%) patients in the age group >60 years had treated for TB with HIV and 1(50%) patient shown high adherence. The Stastiscal analysis has explained [P= 0.1765] that there is no relationship between the treatment response and adherence in age groups. The adherence to treatment is low in patients of the age group 41-60 years.

Adherence According to Gender of Patients

Out of 31 male patients, only 19 (61.29%) were shown high adherence and 4 (12.9%) shown low adherence. Among 21 female patients, 14 (66.67%) were shown high adherence to treatment and only 1 (4.76%) shown with low adherence were shown in Table.4. These values are shown to be statistically significant with a p value is found to be 0.0128, were it implies that the male population are more prone to shown low adherence to treatment. This may due to the variations in the life style factors such as alcohol, smoking, diet and tobacco use.

Table 4: Medication Adherence According to the Gender of Patients(n=52)

Gender	High Adherence	Medium Adherence	Low Adherence	p value
Male(n=31)	19(61.29%)	7(22.5%)	4(12.9%)	

Female(n=21)	14(66.67%)	6(28.57%)	1(4.76%)	0.0128*
Total no. of Patients	34	13	5	

Medication adherence of patients according to their life style factors:

During therapeutic management, this study had analyzed the relationship between the medication adherence and life style factors. Out of 52, patients in smoking category and tobacco chewing category it was observed that there is no statistical difference between the groups ($p=0.1103$ and $p=0.2220$) respectively. In Alcohol consumption it was found to be statically significant ($p= 0.0410$) shown in Table.5.

Table 5: Medication adherence of patients according to their life style factors:

Parameters	No of Patients (%)			p Value
	High Adherence	Medium Adherence	Low Adherence	
Smoking status				
○ Smokers	11	7	2	$p=0.1103$
○ Non-smokers	23	8	1	
Alcohol Consumption				
○ Alcoholics	13	8	2	$p=0.0410^*$
○ Non-Alcoholics	21	7	1	
Tobacco Chewing				
○ Users	9	5	1	$p=0.2220$
○ Non-users	26	9	2	

In the analysis of patient satisfaction about clinical pharmacist intervention,49 patients (94.23%) about medications use,44 (84.61%) regarding Clinical Pharmacist service and 8 (15.38%) dissatisfied with the pharmaceutical care were given in Table.6.

CD4 count and response to DOTS regimen

CD4 cells count of patients before and after taking ATT regimen was shown in Table.6.In pre and post treatment, >200 Cells/ mm^3 in 26 and 25 patients,100-200 100-200Cells/ mm^3 in12 and 15 patients, 50-100Cells/ mm^3 in 10 and 11 patients, <50 Cells/ mm^3 were present in 4 and 1 patients respectively.CD4 cell count examined for 52 patients and the observed values are statically analyzed by using Wilcoxon T test, and the p value was 0.0087 which were significant.

Table 6: CD4 Count of Patients in Response to ATT treatment:

CD4 count	Pre -Treatment(n=52)	Post-Treatment(n=52)	p value
>200 Cells/ mm^3	26	25	0.0087*
100-200Cells/ mm^3	12	15	
50-100Cells/ mm^3	10	11	
<50 Cells/ mm^3	4	1	

Patient Satisfaction of Clinical Pharmacist guidance:

49(94.23%) of patients were satisfied with the explanations given for medications by Clinical Pharmacists,46(88.47%) of patients was happy with the approach of Clinical Pharmacists and spending of time, 44(84.61%) of patients satisfied about the care they have received and 8(15.38%) dissatisfied with healthcare service provided by Clinical Pharmacists were depicted in Table 7.

Table 7: Patient satisfaction questionnaire :(n=52)

QUESTIONS	AGREE	DISAGREE
Clinical pharmacists are good about explaining the reason for medications	49(94.23%)	3(5.76%)
The medication care I have been receiving is just about perfect	44(84.61%)	8(15.38%)
Clinical pharmacists act too businesslike and impersonal towards me	0	52(100%)
Clinical pharmacists sometimes ignore what I tell them	0	52(100%)
I have some doubts about the ability of clinical pharmacist who counsel me	8(15.38%)	44(84.61%)
Clinical pharmacist spends plenty of time with me	46(88.47%)	6(11.53%)
I am dissatisfied with about the medication care I receive	8(15.38%)	44(84.61%)
My clinical pharmacist treats me in a friendly and courteous manner	46(88.47%)	6(11.53%)

DISCUSSION:

Tuberculosis is a communicable and potentially life-threatening disease continued to remain a public health problem particularly in this developing world. The emergence of Human Immune Deficiency Virus infection has led to an increase in incidence of Tuberculosis [10]. Its close association with TB possesses a great challenge in health system.

With the aim of analyzing the response to DOTS Regimen on Opportunistic HIV Infected Patient with Tuberculosis in A Tertiary Care Hospital. Adhikari N et al. did a study in Nepal and found that men, Dalits, and PLHIVs with HIV stage progression had a greater risk of contracting TB [11]. In our study 21-40 & 41-60 age group people were mostly participated, male patients were slightly more than the female patients were included in the study. Around 61.84% patients were nonsmokers, almost equal proportion of alcoholics and non-alcoholics, 71.16% were tobacco non-users. Among the study population 34.64% were illiterate, The Occupation status of patients were scattered from Profession to unemployed, 40.38% were Lower (V) grade as per Kuppasamy socio economic status. (Table 1)

In a study led by Soumya Swami Nathan et al says that Cough and weight loss were the two symptoms of TB with HIV infection that appeared most frequently, followed by fever [12]. Our study results have shown that in response to DOTS Treatments the following Clinical Signs and Symptoms were present, in the Initiation of Treatment 98.07% patients had cough but in the end of the treatment it has been largely diminished to 1.92% of the study population, as the same weight loss, chest pain and fatigue was majorly observed in the starting of the therapy whereas in the end of the therapy all the above inconveniences were remarkably reduced. Fever, Dyspnea, Hemoptysis were fully absent, which indicates the effectiveness of DOTS treatment (Table 2).

Donald E Morisky et al. and Miller et al. in an outpatient environment demonstrated the predictive value of a medication adherence measure. In his study he says that the medication adherence scale is an instrument that can be used to identify patients with their adherence problem [13,14]. The medication Adherence before and after the intervention of clinical pharmacist was found to be effective. In the Low level of adherence was found to be more before the Intervention, which was substantially reduced after the second review. Medium level of adherence was slightly reduced after second review the high level of adherence was considerably increased from 17.03% to 65.38% which denotes that the intervention of clinical pharmacist highly influences the Medication Adherence of the patients, when compared to the male patients the female patients were shown to possess high medication adherence, the males were shown to have low medication adherence. (Table 3&4)

Neeraj et al. investigated that treatment noncompliance could be decreased with repeated counselling and motivating of noncompliant subjects [15]. In our research findings, according to their life style factors of the patients the Non-smokers prone to show high medication adherence that the smokers, the Non-Alcoholics and non tobacco chewers also have showed high medication adherence comparatively to the alcoholics and tobacco chewers. As per the life style factors the health lifestyle patients have seems to be obeying the treatment and getting rid of the disease faster than the bad life style. (Table 5)

Tiburcio R et al. demonstrated that It is well known that the creation of cytokines such TNF-a, which promote viral replication, occurs as a result of tuberculosis, which quickens the advancement of HIV disease [16]. Our study has shown significant results of CD4 cell count between pre and post treatment of ATT regimen in immunosuppressed patients. (Table 6)

Nasir M et al. have found that When a pharmacist educated patients on how to utilise their medications and addressed their concerns with pharmaceutical care, patients' compliance to TB therapy improved [17]. Our study revealed that the patients have agreed that clinical pharmacists are good about explaining the reason for medications and accepted as they received the medication is just about perfect. The entire population didn't find the Clinical pharmacists act too businesslike and impersonal, Clinical pharmacists will never ignore the contents shared by the patient and they were more attentive to their points. They patients have happy about the clinical pharmacist have spent plenty of time with the patients in order to take care of them, have accepted the potential ability of clinical pharmacist. The 84.61% of patients were satisfied about the medication they received. The patients were treated friendly and courteous manner by the clinical pharmacist (Table 7). As per the data received the intervention of clinical pharmacist has significantly increase the patient adherence towards the rational and proper use of medicines which helps them to recover from the disease. Clinical pharmacist enhanced healthcare in increasing response to DOTS Regimen on Opportunistic HIV Infected Patient with Tuberculosis.

CONCLUSION:

A number of characteristics of tuberculosis associated with human immunodeficiency virus infection and its treatment differ from those of TB in patients who are not HIV-positive. Monitoring the CD4 T lymphocyte cell count is essential for assessing the effectiveness of anti-retroviral therapy and the patient's immune system development. Starting therapy for an opportunistic infection like tuberculosis is important. It is important to regularly check on patients' medication compliance and treatment outcomes in HIV-infected patients with tuberculosis in order to enhance their health. A clinical pharmacist's primary responsibility is to inform patients on the proper use of medications and any potential side effects in order to improve their quality of life.

CONFLICT OF INTEREST: The authors declared that they have no conflict of Interest

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References:

1. Naidoo K, Gengiah S, Yende-Zuma N, Mlobeli R, Ngozo J, Memela N, et al . Mortality in HIV and tuberculosis patients following implementation of integrated HIV-TB treatment: Results from an open-label cluster-randomized trial. *EClinicalMedicine*. 2022; 44:101298.
2. Asuke S, Bimba J, Ngutor SM, Ejiga E, Miracle SZ, Anamayi DM. Prevalence of tuberculosis-HIV co-infection and factors associated with treatment outcome among the tuberculosis patients in HIV treatment facility in a teaching hospital in Jos, North Central Nigeria. *Port Harcourt Med J* 2020; 14:119-24.
3. World Health Organization. Global Tuberculosis Report 2020 [Internet]. 2020. Available from: <https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf>.
4. Harries AD, Zachariah R, Corbett EL, Lawn SD, Santos-Filho ET, Chimzizi R, et al . The HIV-associated tuberculosis epidemic—when will we act?. *The Lancet*. 2010;375(9729):1906-19.
5. Selwyn PA, Hartel D, Lewis VA, Schoenbaum EE, Vermund SH, Klein RS, et al. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *New England journal of medicine*. 1989;320(9):545-50.
6. Corbett EL, Charalambous S, Moloi VM, Fielding K, Grant AD, Dye C, et al. Human immunodeficiency virus and the prevalence of undiagnosed tuberculosis in African gold miners. *American journal of respiratory and critical care medicine*. 2004;170(6):673-9.
7. Shete A, Thakar M, Abraham PR, Paranjape R. A review on peripheral blood CD4+ T lymphocyte counts in healthy adult Indians. *The Indian journal of medical research*. 2010 ;132(6):667.
8. Addis Alene K, Nega A, Wasie Taye B. Incidence and predictors of tuberculosis among adult people living with human immunodeficiency virus at the University of Gondar Referral Hospital, Northwest Ethiopia. *BMC infectious diseases*. 2013 Dec;13(1):1-9.
9. Iroezindu MO, Ofondu EO, Mbata GC, Van Wyk B, Hausler HP, Au DH, et al. Factors associated with prevalent tuberculosis among patients receiving highly active antiretroviral therapy in a Nigerian tertiary hospital. *Annals of Medical and Health Sciences Research*. 2016;6(2):120-8.
10. Morens DM, Folkers GK, Fauci AS. The challenge of emerging and re-emerging infectious diseases. *Nature*. 2004 Jul;430(6996):242-9.
11. Adhikari N, Bhattarai RB, Basnet R, Joshi LR, Tinkari BS, Thapa A, et al. Prevalence and associated risk factors for tuberculosis among people living with HIV in Nepal. *Plos one*. 2022;17(1):e0262720.
12. Swaminathan S, Sangeetha M, Arunkumar N, Menon PA, Thomas B, Shibi K, Rajasekar S. Pulmonary tuberculosis in HIV individuals: preliminary report on clinical features and response to treatment. *Indian Journal of Tuberculosis*. 2002;49(4):189-93.
13. Morisky DE, Malotte CK, Ebin V, Davidson P, Cabrera D, Trout PT, Coly A. Behavioral interventions for the control of tuberculosis among adolescents. *Public health reports*. 2001 Nov;116(6):568.
14. Miler M, Šimundić AM. Low level of adherence to instructions for 24-hour urine collection among hospital outpatients. *Biochemia medica*. 2013 Oct 15;23(3):316-20.

15. Rai N, Kushwah SS, Singh SP, Dubey D. An assessment of treatment compliance among patients on DOTS under revised national tuberculosis control programme in district Rewa, Madhya Pradesh, India. Doi:<http://dx.doi.org/10.18203/2394-6040.ijcmph20150961>
16. Tiburcio R, Barreto-Duarte B, Naredren G, et al. Dynamics of T-lymphocyte activation related to paradoxical tuberculosis-associated immune reconstitution inflammatory syndrome in persons with advanced HIV. *Front Immunol.* 2021; 12:757843
17. . Nasir M, Khan MA, Ashiq N, Haroon M, Rukh L, Farooq U. Role of the Clinical Pharmacist in adherence to the treatment of Multidrug-Resistant and Extensively Drug Resistant Tuberculosis. *Pakistan Journal of Chest Medicine.* 2019 Mar 15;25(1):11-6.