

**MEDICATION ADHERENCE TO ANTI TUBERCULOSIS
TREATMENT AMONG TUBERCULOSIS PATIENTS IN AN URBAN
PRIVATE TERTIARY REFERRAL HOSPITAL: A PROSPECTIVE
CROSS SECTIONAL STUDY**

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ABSTRACT

Aim and Objectives: The aim and objective of our study was to investigate the anti- TB treatment adherence rate and to identify factors related to eventual Non Adherence among TB patients during Intensive Phase in an Urban Private Tertiary Referral Hospital using Knowledge Assessment and Medication Adherence Questionnaire. **Materials and Methods:** A prospective cross-sectional study was conducted in a tertiary care hospital for a period of 6 months. Both outpatients and inpatients having Intensive Phase of Tuberculosis were included. Statistical significance was analysed using chi- square χ^2 test with minimum significant level of $p < 0.05$. **Results and Discussion:** Our study comprises of 110 patients out of which most patients were in the age group of 56-70 (23.64%). In our study, 90.9% were adhered to the

TB treatment regimen after 1st follow up and after counselling and education adherent rate was increased on 2nd follow up (94.5%). The reasons for non-adherence was found to be cost of treatment and transport, side effects of TB drugs, irregular visit, irregular intake of drugs. Most common side effects were itching, rashes, increased Liver Function Test. The level of adherence was measured based on modified Morisky scale through which 67.27% were

found to be high adherent, 23.8% were found to be medium adherent, 9% were found to be low adherent. **Conclusion:** Our study suggests that poor background may influence the patient's adherence level. The pharmacist provided patient's education found to have small but significant influence on patient's adherence and health care outcome.

KEYWORDS: Tuberculosis, Adherence, Resistance.

INTRODUCTION

Tuberculosis (TB) is a communicable disease caused by *Mycobacterium tuberculosis*, which can produce either a silent, latent infection or a progressive, active disease.^[1] Other organisms which cause TB includes *M. bovis*, *M. microti* and *M. africanum*. TB is transmitted through air by coughing or sneezing, which is presented as weight loss, fatigue, productive cough, fever, night sweats, frank haemoptysis etc.

India accounts for about a quarter of the global TB burden. In worldwide, India is the country with the highest burden of both TB and Multi Drug Resistant TB (MDR- TB).^[2] There are an estimated 79,000 multi-drug resistant TB patients among the notified cases of pulmonary TB each year. India is also the country with the second highest number (after South Africa) of estimated HIV associated TB cases.^[3]

A WHO fact sheet on tuberculosis stated that overall one third of the world's population (over 2 billion) is currently infected with the TB bacillus. According to it, every second, someone in the world is newly infected with TB bacilli and one in every 10 of these newly infected people will become sick or infectious later in life. TB is one of the top three infectious killing diseases in the world: HIV/AIDS kills 3 million people each year, TB kills 2 million and malaria kills 1 million.^[4]

Major challenges to control TB include illiteracy, didn't understand the purpose of treatment, forgetfulness, not perceiving the treatment as necessary, lack of trust in treatment, lack of knowledge about disease and also patients with psychiatric problems, missing visits, poor relationship with health care provider etc., Also, the emergence of multi drug-resistant TB (MDR-TB) and Extensively drug-resistant TB (XDR-TB) which were resistant to the two most potent anti-TB drugs, viz., Isoniazid and Rifampicin, and the latter to any fluoroquinolone and any of the second-line anti-TB injectable drugs (amikacin, kanamycin or capreomycin) were the major problems in the success of anti- TB treatment.

Medication adherence defined by the World Health Organization as the extent to which a person's behaviours in taking medication corresponds with agreed recommendations from a health care provider.^[5] Adherence is a multidimensional phenomenon determined by the interplay of five sets of factors, termed "dimensions" such as the Social/economic factors, Provider-patient/health care system factors, Condition-related factors, Therapy-related factors and Patient-related factors. Adherence to treatment is challenging, given the complexity, modest tolerability, and long duration of treatment regimens currently available for both drug-susceptible and resistant tuberculosis (TB). In turn, low adherence increases the risk of poor outcomes, including treatment failure, relapse, and development or amplification of drug resistance.^[6]

Hence this project titled “Medication adherence to Anti Tuberculosis Treatment among Tuberculosis patients in an urban private tertiary referral hospital: A prospective cross sectional study” is an attempt made to identify the patient adherence & factors affecting non-adherence during intensive phase and thereby improving overall health care outcomes.

MATERIALS AND METHODS

This was a Hospital Based Prospective Cross-Sectional Study conducted in the Department of General Medicine and Pulmonology at Vijaya Group of Hospitals, Vadapalani, Chennai, Tamilnadu in which a total of 110 patients were enrolled in the study for a period of six months from April 2018 to September 2018. The study was approved by Institutional Ethical Committee of Vijaya Hospital (Ref No: ECR/677/Vijaya/Inst/TN/2013-Re-registration-2016) and includes Confirmed cases with Initial intensive phase of Pulmonary and Extra Pulmonary Tuberculosis, Both In –patients and Out-patients, either gender aged 18 years or older also Associated disease with multiple drugs and excludes Patients aged less than 18 years, Those patients who were mentally incapable of answering due to accompanied mentally diseases during the interview and Patient defaulter.

Collection of data was done by using a specially designed data entry form, which includes information of patient demographic data such as age, gender, education, social history, medication history, Vital signs, diagnosis, Treatment adherence and non-adherence etc.

Questionnaires were used to assess knowledge and adherence towards TB such as

Knowledge Assessment questionnaire:- These questions are concerned to general information about disease, symptoms, purpose and adverse effects of medicine.

Medication Adherence Assessment questionnaire:- Suitably designed MAAQ is prepared by referring Morisky Medication Adherence scale (MMAS 8).

Prior to the study, written consent was obtained from each participant after prospective participants has been fully informed on how the study was carried out and how the collected data was handled to ensure confidentiality and privacy. Each participant had the right to refuse to participate without negative consequences.

Method

Initial Visit: Treatment is initiated when TB is confirmed or strongly suspected and consists of an initial intensive phase for 60 days. During initial visit, consent from the patient was obtained and the demographic details were entered in the data entry form. Face to face Interview was conducted depending on the language of choice of the participants. Patients was advised to come for the first review after 2 weeks. The main indicator to allocate the TB patient adherent or non-adherent was the fact if the patient has forgotten to receive the TB drugs in a period longer than three days.

First follow up: On the day of follow up i.e., on 15th day Phone call was made to the individual patient as a reminder for review. If the patient is unwilling to come, the factors related to it was asked and noticed in the data entry form which was considered as non-adherence. If the patient came for the review, knowledge for patient towards disease and medication adherence was assessed. After assessment, deficit in knowledge and level of adherence was noticed and they were systemically counselled and educated.

Second follow up: During the second follow up (i.e.) on 60th day adherence and non-adherence was monitored and outcome was analysed.

Statistical Analysis

The data collected from the patients through the designed questionnaire format during the interview was entered in Microsoft Excel Spreadsheet and later transported to SPSS for further interpretations. The differences between groups and the proportion of poor adherence for all variables was analysed using chi- square χ^2 test with minimum significant level of $p < 0.05$.

RESULTS

A total of 110 patients who are having Pulmonary or Extra- Pulmonary Tuberculosis were selected for the study based on inclusion and exclusion criteria. Among 110 tuberculosis patients, male patients 58 (52.7%) were more than the female patients 52 (47.2%). The mean age of study population was 45.3 ± 19.6 , where the maximum number of patients fell in the age group between 56-70 years (23.64%) and least number of patients (1.82%) were in the age group of more than 85 years. About 66% (73) patients were underweight, 19% (21) were having normal body weight, 14% (15) were overweight, 1% (1) were obese. More patients 51% (56) were from the urban areas than rural areas, 49% (54).

Patient education is important in Indian setup because many patients are illiterate and comes from a low socio-economic background which plays a role in adherence to the medication. In our study graduates were more 39% and 8% were illiterate. There were 14% smokers, 16% alcoholics and 1% tobacco user. Occupational status is a contributory factor to TB patient's treatment compliance. In our study, unemployed were 29%, employed were 24%, students were 18%, self-employed 15% and retired were 14%. Marital status might influence patient compliance with medication positively. Out of 110 patients 79.09% were married, 19.09% were un married, 1.82% are divorced.

Our study shows pulmonary tuberculosis 79 (72%) were more common than extra-pulmonary tuberculosis 31 (28%) i.e., 72% (79) had TB on lungs, followed by 6% (7) on lymph node, 5% (6) in meningitis, 5% (5) in miliary, 3% (3) in spine, 4% (4) in cervical and abdomen, 1% (1) intestinal & ileocaecal. The co-morbidities present among our study population were Diabetes Mellitus 32% (18), hypertension was about 27% (15), about 18% (10) were having cardiac problems and 23% (13) other disease conditions. The common TB drugs prescribed were Isoniazid, Rifampicin, Ethambutol, Pyrazinamide, Levofloxacin, Streptomycin, Ethionamide, Cyclosporine & Akurit (combination of Isoniazid, Rifampicin, Ethambutol & Pyrazinamide).

Out of 110 patients, 90.9% (100) were adherent to the treatment, while 9.09% (10) were non-adherent after first follow-up. Among the 10 non-adherent patients present in our study, the reasons for non-adherence was found to be socio economic related factors 2%, therapy related factor was 3% and patient related factor was 5%. After first assessment, the reasons for non-adherence were found out and patients were counselled. After 60th day again

adherence rate was measured. Out of 110 patients, 94.5% (104) were adherent to the treatment, while 5.45% (6) were non-adherent to the treatment.

From the modified Morisky Medication Adherence Scale, the level of adherence has been estimated. 67% (74) patients were highly adherent to the therapy, while 22% (24) were medium adherent and 11% were low adherent to the therapy.

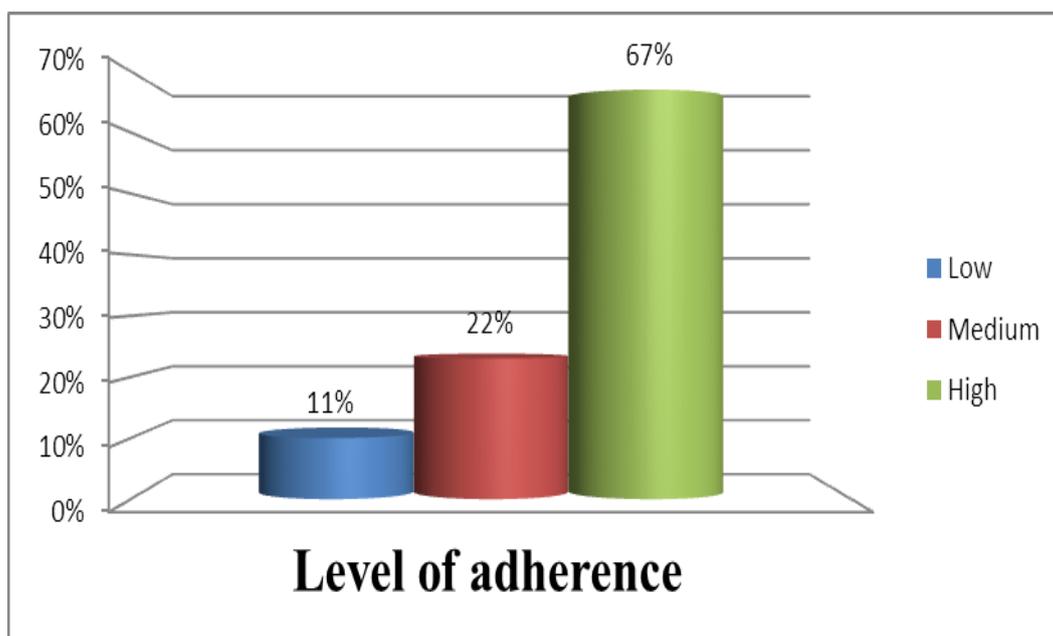


Figure 1 – Level of Adherence.

Socio-Demographic characteristics and adherence level

In our study, there was a significant difference between the adherent and non-adherent group's educational status ($p < 0.043$) with an increased adherence level among graduates as well as in employment status with an increased adherence level in employed compared to self-employed ($p < 0.045$), while other variables such as age, gender, marital status, residence did not affect TB treatment adherence.

Table 1: Socio-Demographic characteristics and adherence level.

Variables	Adherent (n=100)	Non-Adherent (n=10)	Total (n=110) (%)	P-Value
Gender				
Male	50	8	58(52.73%)	0.070
Female	50	2	52(47.27%)	
Total	100	10	110(100%)	
Age				
Less than 25	21	2	23(20.91%)	0.409
25 – 40	24	1	25(22.73%)	
41 – 55	22	2	24(21.82%)	
56 – 70	23	3	26(23.64%)	
71 – 85	9	1	10(9.09%)	
More than 85	1	1	2(1.82%)	
Total	100	10	110(100%)	
Place of Residence				
Rural	47	7	54(49.09%)	0.703
Urban	53	3	56(50.91%)	
Total	100	10	110(100%)	
Marital Status				
Married	78	9	87(79.09%)	0.656
Unmarried	20	1	21(19.09%)	
Divorced	2	0	2(1.82%)	
Total	100	10	110(100%)	
Education				
Graduate	42	1	43(39.09%)	<0.043*
Primary	14	4	18(16.36%)	
Secondary	37	2	39(35.45%)	
Illiterate	7	3	10(9.09%)	
Total	100	10	110(100%)	
Employment				
Unemployed	30	2	32(29.09%)	0.045*
Employed	26	0	26(23.64%)	
Self- Employed	13	4	17(15.45%)	
Retired	12	3	15(13.64%)	
Student	19	1	20(18.18%)	
Total	100	10	110(100%)	

*P <0.05: statistically significant

Knowledge About TB and Adherence Level

Patient knowledge about TB enhances the treatment compliance.

Table 2: Knowledge About TB and Adherence Level.

Variables	Adherent(n=100)	Non-Adherent (n=10)	Total (n=110)(%)	P-Value
What Causes TB				
Do not Know	22	6	28(25.45%)	0.009*
Not True	36	4	40(36.36%)	
True	42	0	42(38.18%)	
Total	100	10	110(100%)	
How TB is Spread				
Do not Know	18	5	23(20.9%)	0.004*
Not True	38	5	43(39.09%)	
True	44	0	44(40%)	
Total	100	10	110(100%)	
How TB is Prevented				
Do not Know	29	5	34(30.91%)	0.133
Not True	46	5	51(46.36%)	
True	25	0	25(22.73%)	
Total	100	10	110(100%)	
Is TB Curable				
Do not Know	27	7	34(30.91%)	0.014*
Not True	24	2	26(23.64%)	
True	49	1	50(45.45%)	
Total	100	10	110(100%)	
Symptoms of TB				
Do not Know	16	5	21(19.09%)	0.025*
Not True	49	4	53(48.18%)	
True	35	1	36(32.73%)	
Total	100	10	110(100%)	

* P < 0.05: statistically significant

Knowledge about TB Drugs and Adherence Level

Out of 110 patients 57.27% patients knew the names of TB drugs, while 65.45% were knew about the daily dosage of TB drugs. Majority of patients knew the colour of TB drugs (93.64%). But the knowledge about side effects of TB drugs was not known much.

In our study, the variables such as the knowledge about names of TB drug were shown to be a difference between adherent and non –adherent group ($p < 0.001$). Also, the knowledge about the length of TB treatment and colour of TB drugs is significantly difference between adherent and non- adherent group ($p < 0.040$ and $p < 0.001$). Other variables in our study had no effects on treatment adherence.

Table 3: Knowledge about TB Drugs and Adherence Level.

Variables	Adherent(n=100)	Non-Adherent (n=10)	Total (n=110) (%)	P-Value
Knowledge about the name of the TB Drug				
Do not Know	18	2	20(18.18%)	<0.001*
Not True	20	7	27(24.55%)	
True	62	1	63(57.27%)	
Total	100	10	110(100%)	
Knowledge about the length of the treatment				
Do not Know	11	1	12(10.91%)	0.040*
Not True	31	7	38(34.55%)	
True	58	2	60(54.55%)	
Total	100	10	110(100%)	
Knowledge about the Daily Dosage of the TB Drug				
Do not Know	15	2	17(15.45%)	0.153
Not True	17	4	21(19.09%)	
True	68	4	72(65.45%)	
Total	100	10	110(100%)	
Knowledge about the Colour of the TB Drug				
Do not Know	1	1	2 (1.82%)	<0.001*
Not True	2	3	5(4.55%)	
True	97	6	103(93.64%)	
Total	100	10	110(100%)	
Knowledge about the Side effect of the TB Drug				
Do not Know	4	25	29 (26.36%)	0.282
Not True	6	55	61(55.45%)	
True	0	20	20(18.18%)	
Total	100	10	110(100%)	

If * P < 0.05: statistically significant

MODIFIED MORISKY SCALE OF ADHERENCE

Among the study population the level of adherence was measured using Modified Morisky medication adherence scale. In our study there is significant association between drug taking behavior and TB treatment adherence such as forgot to take medicine ($p < 0.004$), stopping the medicines when they felt worse ($p < 0.001$), stopping the medicines when felt better ($p < 0.001$), difficulty to take medicines everyday ($p < 0.001$). Non- adherence patients usually ($p < 0.001$) found difficulty in remembering drugs to take.

Table 4: Modified Morisky Scale of Adherence.

Variables	Adherent(n=100)	Non-Adherent (n=10)	Total (n=110) (%)	P-Value
Do you ever forget to take your medication?				
No	95	7	102(92.73%)	<0.004*
Yes	5	3	8(7.27%)	
Total	100	10	110(100%)	
Are you careless at times about taking your medication?				
No	98	5	103(93.64%)	<0.001*
Yes	2	5	7(6.36%)	
Total	100	10	110(100%)	
When you feel worse after taking medicine, do you stop taking it?				
No	95	5	100(90.91%)	<0.001*
Yes	5	5	10(9.09%)	
Total	100	10	110(100%)	
Do you stop taking medication, when you feel better?				
No	97	5	102 (92.73%)	<0.001*
Yes	3	5	8(7.27%)	
Total	100	10	110(100%)	
Do you have any difficulty in continuing your treatment regimen every day?				
No	90	4	94 (85.4%)	<0.001*
Yes	10	6	16(14.5%)	
Total	100	10	110(100%)	
How often do you have difficulty in remembering to take your medication?				
All the Time	0	3	3 (2.73%)	<0.001*
Never/Rarely	77	1	78(70.91%)	
Once in a While	18	1	19(17.27%)	
Sometime	4	1	5(4.55%)	
Usually	1	4	5(4.55%)	
Total	100	10	110(100%)	

* P < 0.05: statistically significant.

DISCUSSION

Tuberculosis is one among the most serious infectious cause of all global mortality and morbidity. Adherence to tuberculosis treatment regimen is a major factor that contributes to its cure rate and better patient health outcomes. Non-adherence to anti TB treatment might trigger TB drug resistance which prolongs the infectiousness of disease and increases the relapse and death of patients.^[7]

This study aims at finding the Anti-tuberculosis treatment adherence rate and to identify the factors related to eventual non adherence among TB patients. The study comprises of 110 patients out of which most patients were in the age group between 56-70 years (23.64%). The

mean age of study population was 45 ± 19 years. In this study male patients 58 (52.73%) were more in number than the female patients 52(47.27%).

Our study results indicate that from 110 interviewed TB patients, 100 (90.9%) were adherent to the TB treatment regimen after 1st follow up (i.e., on 15th day) and after counselling and education adherent rate was increased to 104 (94.5%) on second follow-up. Mahesh Kumar et al in 2002 also reported similar observation of 89.4% compliance rate.^[8] The adherence level in our study was better compared to adherence reported from several studies conducted in different countries with high TB prevalence such as Iran (70%)^[9], Ethiopia (79%)^[10], India (59.5%).^[11] In the present study non-compliance was higher among males 80% than females 20%. In other words, adherence was more prevalent among female patients. The association of compliance with gender is not statistically significant. Suparna Bagchi^[12] et al. also reported non adherence more among male. In our study more patients are from urban areas (50.91%) than rural areas (49%). A dominance of TB patients in urban areas is also reported in other countries like Europe.^[13] It may due to the migration of population from rural towards urban location, which reflected in more TB patients among urban areas.

The non-adherence rate was found to be more among rural patients and between the age group less than 25 year. Similar findings were observed by Kulkarni PY et al., where majority of non-adherent patients were males 15-49 years, and were from lower socio economic status.^[14] Among the 10 non-adherent patients found in the study 9 were married and 1 unmarried. Gortityala S B et al found that 85% of defaults were married.^[15] In our study the non- adherence rate was higher among illiterate. Study conducted by Tachfoutin et al., says that poor literacy level is one of the factor for poor patient compliance.^[16] In our study there is no statistically significant relation between all social demographic factors and non-adherence. However some factors such as education, employment seems to be significantly associated with non-adherence. Similar result were found by study conducted by Tadele Eticha and Eden kassa.^[17] Failure to detect an association between social demographic factors and non-adherence in the survey may occurred due to the small sample size and cross sectional study employed. In our study the reasons for non-adherence was found to be socio-economic related factor such as cost of treatment, cost of transport and therapy related factor such as side effects of TB drugs, patient related factor such as irregular visit, irregular intake of drugs and belief about TB. Most common side effects was itching, rashes, increase LFT. Wares DF et al., also found that adverse effect of ATT was most common of stopping

treatment.^[18] N Jaggarjamma K et- al found that 42% patients stopped the treatment because of ATT induced adverse effects.^[19]

We found that most TB patients lack important knowledge about the disease and its treatment. A high number of TB patients did not answer properly about causes of TB disease, and TB prevention, side effects. Similar findings were observed in a study conducted by Gabriela Fagundez et-al.,^[20] Sophia et al., observed that knowledge about the correct duration of treatment was significantly lower among non- adherent group.^[21] The knowledge about TB drugs such as daily dosages, colour of drugs, length of treatment, names of TB drugs was higher among adherent patients. In this study the level of adherence was measured based on modified Morisky scale, 67.27% were found to be high adherent, 23.8% were found to be medium adherent, 9% were found to be low adherent. The reason for medium and low adherence was found to be forgetfulness, taking medicine every day is difficult to some people, stop taking medicines when felt cure.

Our study results showed that 90% of patients had successful treatment outcomes which is similar to the WHO target of 90% (updated target 2011-2015) though the drugs success rates varied from 86.1 to 95.9% across the health facilities.^[22]

CONCLUSION

Adherence to TB therapy is a complex and dynamic phenomenon. In our study we conclude that out of 110 patients 90.9% were adherent to the drug therapy after first follow up. By providing the education and counselling the adherence rate was increased to 94.5% in second follow-up. In our study the evidence of adherence rate was more in a corporate setup (94.5%) than DOTS (59.6%).^[23] The pharmacist provided patient's education found to have small but significant influence on patient's compliance and health care outcome. In our study the reasons for non-adherence was found to be socio-economic related factor such as cost of treatment, cost of transport and therapy related factor such as side effects of TB drugs, patient related factor such as irregular visit, irregular intake of drugs. Most common side effects was itching, rashes, increase LFT. Various reasons given by patients for non-adherence mostly have the influence of background. People living in rural background and lower strata of society with illiteracy were non adherent. Further study suggests that clinical pharmacist can educate patients regarding their disease and medication. Pharmacist provided patient education helps in better understanding of their disease and medication which will improve of health care outcome of the patient.

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