



Factors Associated with Non-Adherence to Anti-Tuberculosis Treatment Among Patients in Lahore, Pakistan

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ABSTRACT

Introduction: Tuberculosis is a major public health threat that has annihilated more of its infected subjects than any other infectious disease. This study was conducted to explore the factors of non-adherence to anti-tuberculosis treatment along with the socio-demographic indicators. The study also assessed the association between reasons for non-adherence to anti-tuberculosis treatment and the place of living of the patients.

Materials and Methods: This cross-sectional study was conducted in Social Security Hospital, Lahore from September 2020 to June 2021 by interviewing 150 participants receiving anti-TB drugs for at least one month. A semi-structured questionnaire was used to collect information regarding patient's sociodemographics, and factors associated with non-adherence to anti-tuberculosis treatment. A Chi-square test was performed to find out the association between reasons for non-adherence to anti-tuberculosis treatment and place of living using SPSS.

Results: Of 150 participants, 54.7% were males while 45.3% were females having age range between 18 to 80 years. The average duration of anti-tuberculosis treatment was 3.88 ± 1.346 months. The average overall number of anti-tuberculosis treatment doses missed during the last two weeks was 3.23 ± 1.495 . Patients reported that the treatment course was lengthy (99.3%), took more than 15 minutes travel time to reach the health care facility (91.3 %), and felt that their appetite was influenced after taking drugs (90.7%). Patients living in rural areas (52.6%) were more likely to feel poor support from health staff as compared to those who were residing in urban areas (33.3%) which was statistically significant ($p = 0.026$).

Conclusion: The study concluded that the level of education of the patients is associated with the non-adherence to the TB treatment among people living in urban and rural areas. Also, distance of the healthcare facility from residence, travelling time, nature and availability of transport services significantly affect the patient compliance with the TB therapy. Moreover, socioeconomic background, monthly income, and the employment status play an important role in the determination of successful completion of TB treatment by a patient. Whereas multiple drugs for treatment, higher dosages and long duration of treatment also affects the adherence to the treatment plan.

Key Words: Medication Adherence, Anti-tubercular Agents, Therapeutics, Urban Health, Rural Health, Pakistan, Developing Country

INTRODUCTION

TB is one of the peak ten reasons for fatality globally.^{1,2} TB is an infectious malady typically caused by Mycobacterium tuberculosis (MTB) transmitted through droplet infection and predominantly affects the lungs. MTB has a very old history: it has lived for more than 70,000 years in the world.^{2,3,4,5,6} It predominantly affects the lungs but can also affect other organs distinguished by chronic cough with blood-containing mucus, fever, night sweats, and weight loss.^{2,4}

In 2018, internationally, approximately ten million (between, 9.0– 11.1 million) individuals got infected with TB, equal to 132 infected subjects (118–146) per 100,000 residents.⁷ TB is still a public health dilemma in Pakistan.⁴ In Pakistan, not fewer than 70,000 casualties annually can be accredited to TB in the state.^{1,5} TB case fatality ratio in 2018 has been estimated to be 8%. The total TB incidence rate of Pakistan is 256 (per 100,000 population) and the estimated proportion of MDR-TB is 4.2% of new cases while 16% were previously treated. Total TB cases notified in 2018 were 369,548

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which included 45% men, 42% women, and 13% children aged 0-14 years, while 80% of these TB notified cases had PTB. TB treatment coverage (notified/estimated incidence) was 64%.⁷

The prevalence of non-adherence to ATT was 44% (low adherence) and 33% (medium adherence) according to a study conducted at Rawalpindi.¹ A study conducted at Abbottabad showed that 3.52% of patients did not complete their treatment.⁸ Treatment compliance is contemplated to be one of the mainly significant rudiments of chronic ailment management programs, as it is crucial in assuring absolute restoration to health and averting the expansion of resistance to tuberculosis medication.⁹ In almost 50% of individuals with chronic illnesses, treatment is not taken as prescribed.¹⁰

Subjects infected with TB should have compliance of more than 90% to assist the progress of therapy.¹¹ Subjects' compliance to ATT in emergent nations has been approximated to be about 40%.¹² Moreover, the development, as well as transmission of MDR and XDR TB, emphasizes the importance of assisting TB subjects to not omit anti TB dosage.¹¹ Apart from resulting personal impairment, non-compliance exposes the community wellbeing, which might increase the contagiousness and amplify the possibility of TB spread.¹³ In subjects on re-treatment for anti-Tb and understanding regarding the infection, obliviousness, and socio-economic determinants added to the subject's unwillingness to adhere with ATT.^{1,6,14}

Poor compliance to the management of persistent ailments inclusive of tuberculosis is a universal dilemma of huge magnitude.¹¹ TB non-adherence is the most important challenge in TB prevention; fighting non-constancy is the major key and foundation stone of ATT. Poor subject compliance to management schedule is the most important reason for the failure of the treatment and the development of TB drug resistance.^{6,12}

Poor constancy to anti-tubercular prescription i.e., non-compliance is a most important hurdle to its worldwide control.³ Non-compliance to ATT is recognized as one of the chief hindrances against its elimination.¹ The augmented TB burden is because of several determinants inclusive of overlook of TB control by states, unsatisfactory program administration, HIV transmission, impoverishment, increasing number of inhabitants, acquaintance with TB subject, meagre population-based components, migration from high case incidence areas, alcohol dependence, congested staying places, immune-compromised body, medical staff, and expeditious, uncontrolled development of cities.^{4,6} Apart from resulting personal impairment, non-compliance places and exposes the community wellbeing, which might increase the contagiousness and amplify the possibility of TB spread.¹³

Earlier investigation account travel expenses, male sex, poor communication, missing medicine taking, inferior level of education, joblessness, poor livelihood circumstances, lack of social support, drug complications, forgetfulness about medication, avoiding date of meeting at health care setup, stock out of medicines and distance from hospitals have also revealed the impacts on treatment adherence, particularly in more susceptible individuals. This is chiefly due to issues linked with inadequacy, fundamental low health condition, being short of money to pay for health care, insufficient access to health services, and homelessness as the chief components of non-compliance to ATT.^{1,6,12}

A qualitative study performed in India aimed to identify the barriers in TB treatment, highlighted that patients with TB are stigmatized for the disease, they are negatively influenced by their peers regarding medications available in the public healthcare facilities, they face lack of referral by the private healthcare providers and have false perceptions regarding the efficacy of the TB treatment.¹⁵ Another qualitative study conducted in Ukraine determined the perspective of the patients towards TB treatment and its successful completion and stated that the respondents of the study highlighted psychological distress associated with the healthcare settings as well as non-supportive and antagonistic behaviour of the healthcare providers towards the patients as a potential issue in the successful completion of therapy.¹⁶

Non-adherence to tuberculosis treatment is identified as one of the major obstructions towards its eradication.¹⁷ Problems of multidrug-resistant tuberculosis and its further spread have created new and complicated challenges. The role of various socio-demographic factors is considered a significant contributing factor towards non-adherence.^{1,6,12,14} Pakistan ranks fifth among the most affected countries and carries the fourth highest burden of multidrug-resistant cases.^{1,5} There is an urgent need to identify the contributing factors towards non-adherence and the ways and means to deal with those. So, this study explored the factors of non-adherence to anti-tuberculosis treatment in Lahore, Pakistan along with the socio-demographic profile.¹⁸ In addition, the study also explored the association between reasons for non-adherence to anti-tuberculosis treatment and the place of living of the patients.

MATERIALS AND METHODS

This cross-sectional study was conducted at Social Security Hospital, Lahore from September 2020 to June 2021 by interviewing 150 participants. The Ethical Committee of the University of Lahore, Pakistan approved our study (No. IRB-UOL-FAHS/751/2020) and permission was also obtained from Social Security Hospital, Lahore. All participants gave prior informed consent, in written and verbal form.

The sample size for this study was calculated by using the Prevalence of no monthly income as a factor of non-adherence.¹⁹ The sample size was estimated using the formula: $n = Z^2 \frac{1-\alpha}{2} \rho \left(\frac{1-\rho}{d^2} \right)$

Hence sample size (n) calculated was 150 patients with an 8% margin of error. Non-probability purposive sampling was used for the study. This study was carried out in non-metastatic PTB (Pulmonary tuberculosis) confirmed patients (either based on clinical or laboratory examination) aged 18-80 years both male and female who had taken anti-tuberculosis treatment for at least one month from Social Security Hospital, Lahore, and patients who had missed at least one or more prescribed dosage of TB drugs within two weeks at the time of the interview, residing in Lahore, Pakistan. Pregnant and extrapulmonary TB patients, Patients who were mentally sick or seriously ill and Patients who had comorbidities such as Diabetes Mellitus, CVD, Renal diseases, and Liver diseases were excluded.

A three-part semi-structured questionnaire was prepared to assess the factors associated with non-adherence to anti-tuberculosis treatment and other socio-demographic factors including age, gender, place of living, education, monthly income, and employment status. Information about the factors linked with non-adherence due to which patients stopped taking anti-TB drugs like side effects, time to reach healthcare facility, waiting time in a health care facility, lack of social support, poor communication between patient and healthcare providers, and stock out of medicines were included in the questionnaire. The reliability statistics of 15 items concerning the treatment of the patients, health care facility and patient themselves showed a good Cronbach's Alpha value (0.602) showing the data is reliable and acceptable to use for further data analysis.²⁰⁻²²

The data collected was first entered into the Statistical Package for Social Sciences (SPSS). It was then processed, and statistical analysis was done using the SPSS version 25.0. Qualitative variables like gender, education, monthly income, etc. were reported as frequencies and percentages. Quantitative variables like age were reported as mean $\pm$ standard deviation. A Chi-square test was performed to find out the association between reasons for non-adherence to anti-tuberculosis treatment and place of living. A p-value ≤ 0.05 was taken as statistically significant.

RESULTS

Table 1 showed that the average age of the 150 participants was 44.57 ± 18.069 years. The average duration of anti-tuberculosis treatment was 3.88 ± 1.346 months. On average, the total number of anti-tuberculosis treatment doses missed during the last two weeks was 3.23 ± 1.495 .

The majority were male respondents 82 (54.7%) (Table 2). Most of the study participants 69 (46.0%) were illiterate. The monthly household income of the participants showed that 60.0% belonged to lower-class families.

Table 3 demonstrated the response of participants regarding themselves, health care facilities, and treatment. According to the response, rate 99.3% of participants considered that the treatment course was very long. 91.3 % responded that it took more than 15 minutes travel time to reach the health care facility. 90.7% felt that their appetite was influenced after taking drugs.

Table 4 compares the place of living of the patients and potential reasons for non-adherence to anti-tuberculosis treatment. Respondents living in rural areas (52.6%) were more likely to feel poor support from health staff as compared to those who were residing in urban areas (33.3%). Statistically, a significant association was found between the place of living and the tendency to non-adherence to anti-tuberculosis treatment ($p = 0.026$). Table 4 further shows that in total affected the tendency to non-adherence to anti-tuberculosis treatment.

DISCUSSION

Results of the study reflect that the potential barriers can be attributed to the individuals, their socio-demographic, and the healthcare system.¹⁵ The level of education is one of the important parameters in the determination of the success or failure of any treatment modality. Most respondents of this study were not highly educated but had limited educational backgrounds. Results of this study are consistent with another study of a similar nature conducted in India, stating that the majority of the respondents were illiterate, followed by those who had completed primary education, high school and a few were graduates, which also revealed that people with lower educational status and particularly living in the rural areas of the country were more likely to not comply with TB treatment as compared to people with a better level of education and living in urban settings.¹²

The results of this study are also consistent with studies conducted in Indonesia and Kosovo, regarding the barriers associated with non-compliance to the TB treatment, highlighted that along with general educational status, the knowledge about disease and knowledge about the treatment of disease is also of prime importance. Many of the respondents of the study had a high school or lower education and only a few held graduation degrees, which made it difficult for the patients to develop the concept and understand the treatment modalities. People with a better understanding of the disease and having a better knowledge of treatment show better compliance with the treatment modalities.^{16,23}

The study considered monthly income and the payment for the healthcare services for the TB patients as key barriers and highlighted a positive association of both the study variables with the living settings. The same results were reported by other studies conducted in Pakistan and northwest Nigeria which were conducted to determine the barriers and enablers of TB treatment, which also recorded monthly income and payment for the direct medical and non-medical cost as a potential barrier in the successful completion of TB treatment among patients. According to the study, initially, the patients of low socioeconomic status had to face monetary scarcity, hence it is challenging for them to complete the course of therapy along with limited income and poverty due to the disease.^{16,24-25}

Healthcare providers are the point of the centre for the determination of success or failure of any therapy; therefore, the study also took into consideration the response of the healthcare providers to the patients, particularly doctors; revealed a non-significant relationship. The same has been endorsed by other studies that targeted the healthcare-related factors in the determination of successful completion of TB treatment. These studies revealed that the relation of doctors and patients is important to fight Tb effectively, also doctors should counsel the patient appropriately for better adherence to treatment. Furthermore, the studies recommended that the healthcare delivery for TB should be more patient-centric, the inclusion of patients in decision making should be made assured and the system should provide an equal level of treatment to every TB patient.^{16,26-27}

The present study also revealed a negative association of the shortage of drugs and supplies to the rural or urban living setting as a barrier to TB treatment. This result of the study is not in line with other studies of the same nature in the scientific literature. These studies highlighted that the developed countries' continents have better supply chain management of the healthcare commodities, particularly TB and HIV drugs as compared to the rural settings (53 % versus 100 %). These studies also highlighted those issues in the supply chain of healthcare commodities are one of the hurdles in achieving a complete TB eradication target from Europe.²⁸⁻²⁹

Along with the healthcare system-associated factors, other factors are not linked to the healthcare system but have a great impact on the successful completion of the TB treatment and compliance with the TB treatment plan. Such factors majorly include the distance of a healthcare facility from the residence, quality of transportation, travelling time, and waiting hours at a healthcare facility. The present study has shown a significant relationship of all the stated factors with the adherence to the TB treatment and successful completion of the therapy. The results of the study are consistent with the study, conducted in Nepal to identify constraints in

the successful completion of TB treatment and revealed that the majority of the participants of the study stated that distance of the healthcare facility from their residence, travelling time, nature, and quality of transport available and the waiting hours at healthcare facilities is a potential issue in the continuation of TB treatment.³⁰⁻³¹

TB is a chronic disease that requires a long duration of treatment for the complete recovery of a patient. The present study has taken into consideration the duration of TB treatment a potential barrier to non-adherence to the TB treatment. Although the study showed an insignificant effect of the duration to the successful completion of the therapy concerning the living settings, but the result of this study is not consistent with other studies. Studies based on improvement assessment of ATT adherence highlighted that course of TB treatment is too long and proves to be an effective barrier in the discontinuation of treatment without being fully recovered from the infection. Furthermore, the cost of TB medications is expensive which makes it difficult for people in lower-middle-income countries to purchase the therapy for a longer period.^{16,32}

The present study reported that employment and the fear of side effects and adverse reactions due to TB medication both have statistically no significant effect on the non-adherence to the therapy concerning the living settings. This result of the current study is also not consistent with the similar natured studies conducted in Ethiopia and north-west Nigeria highlighted that employment and the fear of side effects or adverse reactions due to medication have a significant effect on non-adherence to TB therapy. The study conducted in Ethiopia also reported the key reason for showing no compliance to the TB treatment and the main reason for not completing the TB therapy was fear of the medicine-related side effects and adverse reactions.^{24,31}

CONCLUSION

The study concluded that the level of education of the patients is associated with the non-adherence to the TB treatment among people living in urban and rural areas. Also, distance of the healthcare facility from residence, travelling time, nature and availability of transport services significantly affect the patient compliance with the TB therapy. Moreover, socioeconomic background, monthly income, and the employment status play an important role in the determination of successful completion of TB treatment by a patient. Whereas multiple drugs for treatment, higher dosages, and long duration of treatment also affects the adherence to the treatment plan.

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Declaration of Interests

We declare no competing interests.

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Conflict of Interest

The authors declare no conflicts of interest.

Authors' Contribution

Ruhamah Yousaf, Saleem M. Rana, Ejaz M.A Qureshi conceived the idea and design the study framework. Asif Hanif, Shumaila Nargus and Muhammad SG. Khan acquired data and made a substantial contribution while designing the study. Tallat A. Faridi and Seemal Vehra reviewed the important intellectual content of the manuscript. All authors approved the final version of the manuscript.

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Table 1: Age, duration of ATT, and number of doses missed for two weeks

Variables	Minimum	Maximum	Mean $\pm$ SD
Age	18	80	44.57 $\pm$ 18.069
Duration of anti-tuberculosis treatment	1	6	3.88 $\pm$ 1.346
Number of doses missed for two weeks	1	7	3.23 $\pm$ 1.495

Table 2: Demographic variables of the participants

Demographic variables	Frequency	Percentage
Gender		
Male	82	54.7
Female	68	45.3
Place of Living		
Urban	93	62.0
Rural	57	38.0
Education		
Illiterate	69	46.0
Under matriculation	36	24.0
Matriculation (10th Grade)	30	20.0
Intermediate (12th Grade)	11	7.3
Graduation	4	2.7
Employment Status		
Employed	45	30.0
Unemployed	105	70.0
Monthly household income		
Lower class	90	60.0
Middle class	54	36.0
High class	6	4.0

Table 3: Responses of participants regarding themselves, health care facility, and treatment

Questions	Responses	
	Yes (%)	No (%)
Related to the patient		
Do you feel depressed for having the disease?	127(84.6)	23(15.3)
Do you ever forget to take your medications?	120(80)	30(20)
Do you feel your appetite is influenced after taking drugs?	136(90.7)	14(9.3)
Do you sometimes feel that disease condition has not been alleviated and drugs seem to be ineffective?	59(39.3)	91(60.6)
Is the Tuberculosis reference unit far from your home?	135(90.0)	15(10.0)
Does it take > 15 minutes travel time for you to reach the health care facility?	137(91.3)	13(8.6)
Do you perceive that transport to the health centre is difficult due to distance or costs?	132(88.0)	18(12.0)
Related to the health care facility		
Is the waiting time for a medical consultation longer than 60 minutes?	105(70.0)	45(30.0)
Do you ever feel poor support from health staff?	61(40.7)	89(59.3)
Related to the treatment		
Do you consider that the amount of tuberculosis drugs you are taking is too much?	135(90.0)	15(10.0)
Do you perceive that the costs of tuberculosis treatment are too high?	93(62.0)	57(38.0)
Have you ever stopped taking medication due to tuberculosis therapy side-effects?	117(78.0)	33(22.0)
Have you ever stopped taking tuberculosis drugs due to drugs shortage?	10(6.7)	140(93.3)
Have you ever felt any discomfort after taking your tuberculosis drugs?	125(83.0)	25(16.0)
Do you consider the treatment course is very long?	149(99.3)	1(0.7)

Table 4: Association between reasons for non-adherence to anti-tuberculosis treatment and place of living

Reasons for non-adherence to anti-tuberculosis treatment	Place of Living		p-value*
	Urban n (%)	Rural n (%)	
Feel poor support from health staff			
Yes	31(33.3)	30(52.6)	0.026
No	62(66.7)	27(47.4)	
Sometimes feel that disease condition has not been alleviated and drugs seem to be ineffective			
Yes	29(31.2)	30(52.6)	0.010
No	64(68.8)	27(47.4)	
Tuberculosis reference unit far from your home			
Yes	79(84.9)	56(98.2)	0.010
No	14(15.1)	1(1.8)	
It takes >15 minutes travel time for you to reach the health care facility			
Yes	81(87.1)	56(98.2)	0.018
No	12(12.9)	1(1.8)	
Transport to health center is difficult due to distance or costs			
Yes	77(82.8)	55(96.5)	0.018
No	16(17.2)	2(3.5)	

*Chi-square test