Original article

# Factors Affecting Tuberculosis Treatment Adherence among Newly Diagnosed Patients Attending TB Clinic at Tertiary Care Hospital, Lahore

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## ABSTRACT

Background: Pakistan ranks fifth among high tuberculosis (TB) burden countries. Despite Directly Observed Treatment Short Course Strategy (DOTS) implementation, adherence is still poor and Pakistan stood fourth in multi-drug resistant (MDR-TB) cases. This study was conducted to assess tuberculosis treatment adherence among newly diagnosed pulmonary TB patients at TB clinic of tertiary care hospital, Lahore, and to study factors affecting it.

Patients and methods: Between May 2021 and February 2022, cross-sectional study was conducted at outdoor based TB Clinic, Services Hospital, Lahore, interviewing 732 active pulmonary TB patients aged 18 to 65 receiving Anti Tuberculosis Treatment (ATT) for at least two months. Adherence was studied incorporating Morisky Medication Assessment Scale (MMAS) and World Health Organization multi-dimensional adherence model (WHO-MAM) in close-ended questionnaire, considering socio-demographic, patient, health system, and therapy-related factors. Those scoring < 6 on MMAS were categorized low adherents. SPSS Version 25 analysed data. Chi-square test and binary logistic regression explored adherence associations, with $p<0.05$ considered significant.

Results: Out of 732 patients,350 (47.8%) males and 382 (52.2%) had mean age of 37.41±13.3 and 38.80±14.08 years respectively, with family income of 22062.86±19915.34 vs 23900.52±22153.02 rupees, knowledge score of 4.62±1.56 vs 4.68±1.55 and MMAS score was 6.57±1.21 vs 6.59±1.22 respectively. Low Adherence was in 64.2%.After adjusting, significant factors were age (AOR=12.378, 6.679-22.94), being unemployed (AOR=2.18, 0.253-0.815), low income (AR=2.678, 1.29-5.56), doctor's availability (AOR=0.161, 0.067-0.383), non-co-operative staff (AR=6.902,3.197-14.889), distance travelled (AOR=12.056, 5.875-24.74), and adequate knowledge (AOR=3.583,1.699-7.557)

Conclusion: Two-thirds (64.2%) of TB Clinic attendees had low adherence. Unemployment, older age, low income, and inadequate knowledge had higher odds of low adherence. Similarly non-cooperative staff and distance from facility significant affected adherence.

Keywords:

Tuberculosis, Medication Adherence, Morisky Medication Assessment Scale, Factors

## INTRODUCTION

Tuberculosis (TB) is preventable and curable. However, in 2022, TB became second leading cause of mortality after coronavirus disease outpacing HIV/AIDS. This highlighted magnitude particularly in low middle-income countries (LMIC) like Pakistan who ranked 5th among high burden countries,[1,2] stood 4th in MDRTB.[3,4] WHO estimated only half patients adhere to prescribed medications, making it public health priority.[5-7] Interruption to anti tuberculosis treatment (ATT) even once skyrocketed chances of developing MDTR.[6,7] Although TB-DOTS ensured patients' adherence to ATT[8], its challenging implementation depended on resources, settings and environment.[6,7] Literature depicted low ATT adherence in upto 44% Pakistani,[9] 50% Indians, 26.8% Chinese, 15.5% in Thailand, and 35% in Africa,[10] soaring socioeconomic and psychological cost.[11]

Treatment adherence is complex, multidimensional phenomenon interplayed by factors, namely, socio-demographics, healthcare system, therapy and individual characteristics comprehensively described by WHO-MAM.[12,13] These dimensions included socio-demographics, patient, therapy, health system and clinical factors.[12,13] In absence of "gold standards" to determine adherence, MMAS is self-reported, eight item questionnaire tool with good reliability and validity in low-income settings (Cronbach $\alpha$=0.81).[14, 15]

Despite considerable efforts and investments in TB prevention and control, tangible results are still awaited.[4,9,16] The critical importance of treatment

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adherence in disease control cannot be overstated. Understanding adherence presents an opportunity for tailored interventions to address patient behaviour. While evidence on adherence and its socio-demographic correlates is increasing, local literature to study contributing factor awaits attention. This study aimed to assess anti-tuberculosis treatment adherence among recently diagnosed pulmonary TB patients at Services Hospital, Lahore, and to study factors affecting it.

## PATIENTS AND METHODS

It is cross sectional analytical study conducted during May 2021 till February 2022. The data was collected from TB Centre at Services Hospital Lahore after formal permission from Institutional Review Board. A sample size of 380 was calculated with confidence interval of 95% with anticipated non-adherence frequency to medication (44.6%) in Pakistan.[9] However, it was increased to 732 as the study data collection period extended over six months. Newly diagnosed drug sensitive pulmonary TB patients prescribed ATT in last two months, between ages 18-65 years, irrespective of their gender, attending outdoor TB clinic and were willing to participate were included in the study through simple random sampling technique. Pregnant females, default cases, those having co-infections with HIV and with MDR-TB were excluded from due to resource and accessibility constraint.[2]

Close-ended, structured questionnaire administered in patients' language by researcher themselves in same tone and duration, was used for data collection. The study questionnaire was composed of 4 sections. The sociodemographic characteristics measured in section A involving gender, age, marital status, education level, occupation, self-reported average monthly income and chronic illness such as diabetes mellitus, hypertension etc. Section B investigated about health services provision that included questions such as doctor availability, behaviour of staff, expensiveness of medication, its affordability and availability, as well as side effects. Section C evaluated the patients knowledge about tuberculosis that comprised of multiple questions such as cause, spread, symptoms, prevention, cure, name of anti-tuberculosis drugs, length of treatment, daily medicine dosage, side effects of medicines and fatality of untreated TB. One point was given for each correct answer and zero point was given for incorrect answers to the knowledge questions. The patients who scored 8 of these 10 on the questions, had adequate knowledge and those who scored less than 8 had inadequate knowledge.[3] Section D assessed adherence using Morisky Medication Adherence Scale (MMAS-8).[5,15-19] The scale consists of eight items that measure a specific medication behaviour. The patients who scored 8 points were considered as highly adherent those scoring from 6-8 were moderately adherent and below 6, were categorized as low adherent.[10] Adherence was dichotomized and patients were classified as high adherent or low adherent using score 6 as cut off in MMAS-8.[11,15] This scale had good reliability and sensitivity scoring Cronbach's alpha for each section from 0.75-0.83 indicating its internal consistency.[19] Those who claimed to read and write were taken as literate and those earning <250 US Dollar per month were taken as from low income group.[20] The data was collected by a team of researchers. It took almost six months working four days a week from Monday to Thursday and collecting mean sample of 15 patients daily. The collected data was entered cleansed and analysed on Statistical Package for Social Sciences version 25 and presented in the form of tables. The relationship of adherence with socio-demographic profile, health services provision and knowledge was analysed by cross-tabulation and Chi Square test was used as a test of significance with p-value <0.05 was taken as significant. Those having significant p-values in univariate analysis were adjusted for confounders through binary logistic regression.[21] All ethical considerations ensured at every step of this study. Autonomy of the respondents along with confidentiality of data was ensured.

## RESULTS

Among 732 respondents, there were 350 (47.8%) males and 382 (52.2%) were females having mean age of 37.41±13.3, family income of 22062.86±19915.34 rupees, knowledge score of 4.62±1.56 and Morisky Medication Adherence Scale (MMAS) score was 6.57±1.21 among males and females showed mean age of 38.80±14.08, family income of 23900.52±22153.02 rupees, knowledge score of 4.68±1.55 and MMAS score was 6.59±1.22; The respondents living in urban areas were 396 (54.1%) and 586 (80.1%) were married, 222 (30.3%) were unemployed and 510 (69.7%) employed, 20 (2.7%) were self-employed, 28 (3.8%) were retired whereas 54 (7.4%) were students. Regarding education, 226 (30.9%) participants were illiterate, 654 (89.3%) individuals were having low income and chronic illness was present among 400 (54.65%) participants. There were 190 (26%) smokers. The Figure 1 shows that

Table 1: Relationship between socio-demographic profile, and comorbidities with treatment adherence (N=732)

| Variables<br>Sociodemographic Profile | Low adherence (N=470)<br>Frequency (%) | High adherence (N=262)<br>Frequency (%) | Total<br>(N=732) | p-value*<br>Chi-square |
|---|---|---|---|---|
| **Age** | | | | |
| 18-44 years | 52 (40.6%) | 76 (59.4%) | 126 | <0.0001* |
| 45 years and above | 418 (69.2%) | 186 (30.8%) | 604 | 37.54 |
| Mean age + SD in years | | 38.14±13.73 | | |
| **Gender** | | | | |
| Male | 222 (63.4%) | 128 (36.6%) | 350 | 0.700 |
| Female | 248 (64.9%) | 134 (35.1) | 382 | 0.177 |
| **Occupation** | | | | |
| Unemployed | 162 (73%) | 60 (27%) | 222 | 0.001* |
| Employed | 308 (60.4%) | 202 (39.6%) | 510 | 10.65 |
| **Education** | | | | |
| Illiterate | 156 (69%) | 70 (31%) | 226 | 0.07 |
| Literate | 314 (62.1%) | 192 (37.9%) | 506 | 3.304 |
| **Marital status** | | | | |
| Married | 384 (65.5%) | 202 (34.5%) | 586 | 0.135 |
| Single | 86 (58.9%) | 60 (41.1%) | 146 | 2.232 |
| **Residence** | | | | |
| Urban | 246 (62.1%) | 150 (37.9%) | 396 | 0.216 |
| Rural | 224 (66.7%) | 56 (33.3%) | 336 | 1.634 |
| **Income** | | | | |
| Low(<250 USD/month ) | 432 (66.1%) | 222 (33.9%) | 654 | 0.003* |
| Middle or above(> 250 USD/month) | 38 (48.7%) | 40 (51.3%) | 78 | 9.115 |
| Mean ± SD | | 43021.86±21118.38 PKR per month | | |
| **Co-morbidities** | | | | |
| Yes | 256 (64%) | 144(36%) | 400 | 0.898 |
| No | 214 (64.5%) | 118 (35.5%) | 332 | 0.016 |

Table 2: Relationship between health system, patient and therapy related factors with treatment adherence (N=732)

| Variables | Low adherence (N=470)<br>Frequency (%) | High adherence (N=262)<br>Frequency (%) | Total<br>(N=732) | p-value<br>Chi-square |
|---|---|---|---|---|
| **Health System Related Factors** | | | | |
| **Availability of doctor** | | | | |
| Yes | 440 (65.3%) | 234 (34.7%) | 674 | 0.046* |
| No | 30 (51.7%) | 28 (48.3%) | 58 | 4.271 |
| **Affordability of medicines** | | | | |
| Yes | 192 (67.6%) | 92 (32.4%) | 284 | 0.133 |
| No | 278 (62.1%) | 170 (37.9%) | 448 | 2.331 |
| **Availability of medicines** | | | | |
| Yes | 428 (66.5%) | 216 (33.5%) | 644 | 0.01* |
| No | 42 (47.7%) | 46 (52.3%) | 88 | 11.821 |
| **Distance of TB referral unit** | | | | |
| <5km | 32 (16.7%) | 160 (83.3%) | 192 (26.23%) | <0.0001* |
| >5km | 438 (81.1%) | 102 (18.9%) | 540 (73.77) | 255.963 |
| **Behaviour of staff** | | | | |
| Cooperative | 26 (12.7%) | 178 (87.3%) | 204 | <0.0001* |
| Non-cooperative | 444 (84.1%) | 84 (15.9%) | 528 | 325.921 |
| **Counselling about disease and treatment** | | | | |
| Yes | 334(65.2) | 178 (34.8%) | 512 | 0.377 |
| No | 136(61.8%) | 84 (38.2%) | 220 | 0.781 |
| **Patient related factors** | | | | |
| **Knowledge[1]** | | | | |
| Adequate | 36 (15.7%) | 194 (84.3%) | 230 | <0.0001* |
| Inadequate | 434 (86.5%) | 68 (13.5%) | 502 | 344.06* |
| Mean score + SD4.65±1.55 | | | | |
| **Disappearance of symptoms means stopping of medicine** | | | | |
| Yes | 180 (69.8%) | 78 (30.2%) | 258 | 0.024* |
| No | 290 (61.2%) | 184 (38.8%) | 474 | 5.359 |
| **Perceived side effects of the medicine** | | | | |
| Yes | 416 (82.5%) | 88 (17.5%) | 504 | <0.0001* |
| No | 54 (23.7%) | 174 (76.3%) | 228 | 236.620 |
| **Therapy related factors** | | | | |
| **Expensive of the medicine** | | | | |
| Yes | 335 (70.4%) | 141(29.6%) | 476 | **<0.0001*** |
| No | 135 (52.7%) | 121 (47.3%) | 256 | **22.55** |

*The p-values are less than 0.05 and are significant; 1. Knowledge termed as adequate when respondent scored ≥80% on knowledge section of pre-tested questionnaire.

Table 3: Binary logistic regression and adjusted odd ratio of various factors with treatment adherence

| Significant Variable | Crude Odds Ratio | Adjusted Odds Ratio | 95% Confidence Interval | Adjusted p-value |
|---|---|---|---|---|
| Age | 3.285 | 12.378 | 6.679,22.94 | <0.0001* |
| Occupation | 1.771 | 2.188 | 0.253,0.815 | 0.008* |
| Low income | 2.048 | 2.678 | 1.290,5.560 | 0.008* |
| Available of doctor | 1.755 | 0.161 | 0.067,0.383 | <0.0001* |
| Availability of medicine | 2.170 | 1.265 | 0.551,2.904 | 0.579 |
| Expensiveness | 1.308 | 0.866 | 0.490,1.532 | 0.621 |
| Non cooperative behaviour of Staff | 36.187 | 6.902 | 3.197,14.889 | <0.0001* |
| Travel Distance more than 5km | 21.471 | 12.056 | 5.875,24.740 | <0.0001* |
| Inadequate Knowledge of the disease | 34.394 | 3.583 | 1.699,7.557 | 0.001* |
| Perceived of the side effects | 1.464 | 2.45 | 0.211,0.789 | 0.008* |
| Perception about stoppage of treatment | 15.23 | 0.749 | 0.422,1.328 | 0.323 |

*p<0.05 taken as significant

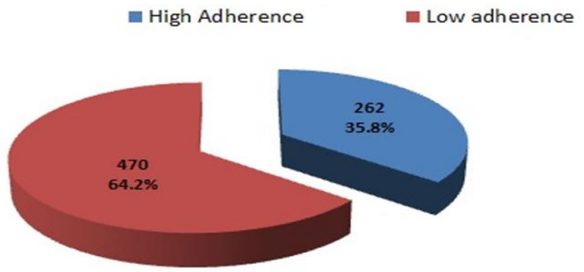


Figure 1: Frequency distribution of respondents' according to treatment adherence (N=732). Low Adherence: Score <6 on Morisky Medication Adherence Scale-8 (MMAS-8). High Adherence: Score > 6 on Morisky Medication Adherence Scale-8 (MMAS-8).

64.2% having low TB adherence. Table 1 showed that overall mean age was 38.14±13.73 years, monthly income was 43021.86±21118.38 rupees. Mean knowledge score was 4.65±1.55 and MMAS was 6.58±1.22; A significant difference of TB adherence was found with higher age (>45 years) (69.2%; p<0.0001), unemployment (73%; p=0.001), low income (62.7%; p=0.017) and insignificant difference found with TB adherence having female gender (64.9%; p=0.700), illiteracy (69%; p=0.07), marital status (65.5%; p=0.135), living in rural areas (66.7%; p=0.216), and co-morbidities (64%; p=0.898).

Table 2 showed that among health system factors, significant association of low adherence with doctor availability (65.3%; p=0.046), medicine availability (66.5%; p=0.01), TB referral unit distance (>5 km) (81.1%; p<0.0001), non-cooperative staff behaviour (84.1%; p<0.0001), inadequate knowledge (86.5%; p<0.0001), symptoms disappearance stop medicine (69.8%; p=0.024), perceived medicine side effects (82.5%; p<0.0001), expensive medicine (70.4%; p<0.0001) and insignificant difference found with TB adherence having medicine affordability (66.5%; p=0.133) and counselling (65.2%; p=0.377).

Table 3 showed that on applying logistic regression, the model indicating significant adjusted odds ratio for age was 12.378 (6.679-22.94), occupation was 0.454 (0.253-0.815), income was 2.678 (1.29-5.56), doctor availability was 0.161 (0.067-0.383), staff behaviour was 6.902 (3.197-14.889), distance travel was 12.056 (5.875-24.74), knowledge adequacy was 3.583 (1.699-7.557), side effects perception was 0.408 (0.211-0.789) and insignificant adjusted odds ratio with medicine availability was 1.265 (0.551-2.904), expensiveness was 0.866 (0.490-1.532) and stop treatment perception was 0.749.

## DISCUSSION

The adherence to the treatment protocol is a critical challenge faced by most of the TB control programs of developing countries.[4] The following cross sectional study results, only 35.8% enrolled TB patients exhibited high adherence. Although Adisa and his co-workers mentions adherence to be as low as 40% in developing countries, this study further presents a gloomy picture.[22] Kosar Aziz and her colleagues also reported similar observation where 21.6% had high adherence and 79% had low adherence.[9] However Farman and his colleagues and found 50.9%of settlements in Baluchistan had high adherence.[4] Poor adherence makes it difficult for Pakistan to achieve world Health Organization target of treatment success of 85%.[4] Strict adherence cut offs and COVID-19 pandemic repercussions might be the reasons of these values argued the shifting of focus and health system

machinery, neglecting many other targets in the unfamiliar scenario that mankind faced. [23]

This study aims to study relationship of various factors and adherence. It is a well-established fact that adherence is multifactorial and multi-dimensional and study of single entity would not fulfil the quest for answers.[8] In patients related factors, among socio-demographics, age, and employment status were found to be significantly relate. Older age, unemployment and low income had higher odds of low adherence with AOR12.3, 2.188 and 2.678 respectively. Over the years the literature showed reduced role of literacy, gender and age in adherence and interventions.[11] However, Turcu et al., found that women and higher education play better adherence to medications than men and less educated patients while age and occupation did not play any significant role in adherence.[24] Arif and his co-workers showed that education alone and income alone would not guarantee favourable treatment outcomes. Health literacy and awareness sessions need to be incorporated to counter these dilemmas.[25] Similarly, smoking, history of co-morbities and marital status had insignificant relationship with adherence which is consistent with Fernandez et al.,[5] However Gozde et al., concluded that older patients with multiple morbidities had higher risk for treatment non-adherence.[26] It is worth noting that in this study non-adherence was more prevalent in older group and only half of the patients had co–morbidities. For patients, correct understanding and knowledge of their disease, its treatment regimens, could be a challenging.[8] Fernandez et al, found that patients with chronic diseases had more hurdles in understanding health care providers' information and was a strong predictor of adherence.[5] Similarly, they concluded that complete treatment information (3.89, 95% CI 2.09–7.21), having adequate knowledge about medication regimen (4.17, 95% CI 2.23–7.80) was significantly related to adherence.[5] This was similar to the results of the following study where adequate knowledge but not the providers' information, were found to be significantly associated with adherence (AOR3.583, CI1.699,7.557, p-value<0.001) which further demonstrates 'one size doesn't fit all' notion. Similar results were found by Arif and his team who showed health literacy, tailored made strategies, patient centric approach need to be incorporated besides imparting only structured messages and knowledge.[5,26] Michalski et. al., also concluded that although better knowledge is related to a higher degree of readiness but it did not influence the compliance of therapeutic recommendations.[27] These observations clearly indicated that correction and out doing one factor would not help Pakistan in halting tuberculosis epidemic. A holistic patient centred approach needs to be embedded in health care system is the need of the hour.

According to the World Health Organization (WHO), number of factors, determine patients' compliance to recommended treatment correctly. Among these, health-care team and system-related played an important role.[5] Distance of TB referral unit more than 5km from place of residence, availability of the doctor and behaviour of the staff were strongest significant factor. This clearly shows a shift in patients' care whereas health system policies limited itself to the affordability and accessibility of the facility. The lack of responsiveness' to patient needs beyond the provision of a material needs was also felt by Abbas et. al., Kosar Aziz and her fellows [7,9] Chen et. al., concluded that good patient-doctor relationship, resulted in satisfaction which in turn resulted in adherence to treatment.[17]

Xu Chen et. al., in 2019 also observed that patients who suffered side effects of medicines were likely to have low adherence level (p= 0.001).[17] Perception and patients' beliefs in continuation of treatment play an important role. Individual and societal perceptions regarding disease, its management, cure and perceived treatment benefit over its influenced factors for non-adherence to TB medication.[8] Gozde et al., found that the patients with chronic diseases were more concern about the necessity of drug and its possible side effects than overuse and treatment harm.[26] Similarly, Fernanadez et al. concluded that perception of the quality of life and medication adherence is related which in turn attributed to psycho-social characteristics.[5]

Nevertheless, this study was an attempt to study the multi-dimensional nature of treatment adherence and factors influencing it, in limited resources. However it was not without limitations. The use of self-report questionnaires in the study, added recall bias or over information bias to some extent. Direct observed methods to study treatment adherence could not be used due to resource constraints. The levels of TB knowledge and perception towards medication among patients were studied, but the ways of acquiring knowledge and detailed effect of beliefs and perceptions on adherence through qualitative research was beyond the scope of this study. Similarly, the study was limited to a single, urban setting and attached to an institutional hospital, resulting in limitations in the diversity of lifestyles, cultural and their influences could not be

discussed. And lastly to study the causal and temporal relationships, a better study design preferably a longitudinal one would be helpful in formulation interventions and recommendations in the light of applied research.

## CONCLUSION

High non-adherence is observed in newly diagnosed TB patients in an urban setting which shares a huge part of global burden of tuberculosis. Older unemployed patients of either gender were more non-adherent. Similarly health system related factors such as unavailability of the doctor, expensive medicines, inaccessibility and non-cooperative behaviour of the staff resulted in non-adherence despite good adequate knowledge of disease and its management. Incorporation of tailored strategies, adoption of patient-centred approach and monitoring and accountability are the only weapons left for the country to fight TB epidemic and horror of MDR-TB.

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