

Barriers to Treatment Compliance of Directly Observed Treatment Shortcourse among Pulmonary Tuberculosis Patients

Sujan Babu Marahatta,¹ Rajesh Kumar Yadav,² Sushila Baral,² Neeta Aryal,² Srijana Poudel,³ Naveen Prakash Shah,⁴ Punita Yadav,⁵ Suman Chandra Gurung,⁶ Elina Khatri⁷

ABSTRACT

Background: Treatment compliance is an important aspect for tuberculosis prevention and control. Poor compliance to treatment can lead to the development of drug-resistant tuberculosis. The aim of this study was to explore the factors affecting treatment compliance for tuberculosis patients.

Methods: Facility based unmatched case control study was done among the forty non-compliance and eighty compliance pulmonary tuberculosis patients registered at selected directly observed treatment short-course centers of six districts. Data were collected using in-depth interview guideline with the tuberculosis focal person and Focus Group Discussion with tuberculosis patients.

Results: A total of 120 respondents, 40 cases and 80 controls were enrolled in the study. About 72.5% of the cases and 56.2% of the controls were male. Five significant independent risk factors for non-compliance to TB treatment were identified. The qualitative session confirmed geographical barriers, inaccessibility to health facility, economic barriers, difficulty in convincing people, knowledge about Directly observed treatment shortcourse program, longer medication period, migration and stigma as a major barrier for treatment compliance.

Conclusions: Wider ranges of barriers are prevalent in context of tuberculosis treatment pathway and outcome. Knowledge of the tuberculosis patients and attitude of the family plays a vital role in treatment compliance. Directly observed treatment shortcourse playing tremendous role to ensure treatment adherence has been identified as major barrier to adherence as well. Enablers of adherence need to be emphasized to address the barriers.

Keywords: Barriers; DOTS; mixed method; Nepal; treatment compliance; tuberculosis

INTRODUCTION

Tuberculosis is the ninth leading cause of death worldwide from a single infectious agent.¹ It is estimated that 95 % tuberculosis cases and 98% of tuberculosis death occur in the South Asia.² Fuelled by poverty, poor public health systems, and increasing HIV/AIDS prevalence, tuberculosis continues to be a persistent challenge for global health and development.³

The difficulty experienced by patients following a particular treatment regimen has raised awareness of compliance.⁴ Socioeconomic, patient-related, life-style, condition related and co-morbidity have been identified as competing causes for patients' non-compliance to tuberculosis treatment.⁵⁻⁹

Efforts to improve medication outcomes require a better understanding of compliance as a complex behavioral

issue and particular barriers and facilitators of patient compliance. Direct observation by health workers reduce the risk of treatment non-compliance.¹⁰ In addition, poor treatment compliance lead to development of drug resistant tuberculosis.¹ The aim of study was to explore the factors affecting treatment compliance for tuberculosis patients in Nepal.

METHODS

A mixed method study was conducted with quantitative facility based unmatched case control (1:2) and qualitative sequential exploratory study. This study was done in six districts representing each geographical region of Nepal to determine the factors affecting treatment compliance and explore associated factors. 40 non-compliance (cases) and 80 compliance (controls) TB patients were recruited in the study from the list obtained from DOTS center with high caseload using

Correspondence: Sujan Babu Marahatta, Manmohan Memorial Institute of Health Sciences, Kathmandu, Nepal. Email: sujanmarahatta@gmail.com, Phone: +9779851126707.

simple random sampling. For this study, pulmonary bacteriology confirmed tuberculosis patient whose treatment was interrupted for 2 consecutive months or more were included as non-compliance and those tuberculosis patients who has smear or culture-negative in the last month of treatment and on at least one previous occasion were included as compliance tuberculosis patients. Face to face interview was done to collect quantitative information.

Furthermore, in qualitative component six Focus Group Discussions (FGDs), one each in a district were conducted among tuberculosis medication patients. Twelve in-depth interviews were conducted with government health service providers at various levels including DOTs and DTLO focal persons. Participants for qualitative study were recruited by using purposeful sampling strategies. Field notes were recorded immediately after the interview. All in-depth interviews were recorded, transcribed and translated into English. The content and theme analysis was conducted with the consultation of interviewer, principal investigator and independent reviewer.

Quantitative data was entered in EPI Data and transferred to SPSS for the analysis. Multi-variate logistic regression analysis was performed to assess the independent factors among those showing statistically significant in bivariate analysis ($P < 0.05$). A codebook of themes and subthemes were created to code qualitative data. Coded qualitative data was then synthesized using inductive techniques and reviewed by two researchers for consistency and thematic analysis was performed. Where appropriate, additional quantitative frequencies were generated from qualitative data to tabulate the magnitude of specific comments made on various themes and subthemes. The qualitative data were transcribed and looked for patterns among the participants. The thematic analysis of transcriptions was done using qualitative data analysis software.

Ethical approval was taken from Nepal Health Research Council (NHRC). The verbal approval from concerned authorities of respective district (public) health office was obtained prior data collection. All compliance and non-compliance participants were explained about voluntary participation and right to withdraw at any time from the study. Written informed consent was signed by both interviewer and participants before the start of the study.

RESULTS

The socio-demographic characteristics of study participants are illustrated in Table 1 which showed

that most of the respondents (86.7%) had visited public treatment center. About three-fifth (61.7%) respondents were male.

Table 1. Socio-demographic characteristics of the participants.

Characteristics	Total	Compliance	Non-Compliance
Treatment Centre			
Public	104(86.7)	72 (90.0)	32 (80.0)
Private	16 (13.3)	8 (10.0)	8(20.0)
Ecological Region			
Mountain	3 (2.5)	0 (0.0)	3 (7.5)
Hilly	68 (56.7)	47 (58.8)	21 (52.5)
Terai	49 (40.8)	33 (41.2)	16 (40.0)
Gender			
Male	74 (61.7)	45 (56.2)	29 (72.5)
Female	46 (38.3)	35 (43.8)	11 (27.5)
Age			
15-40 Years	74 (61.7)	53 (66.2)	21 (52.5)
40-65 Years	38 (31.7)	22 (27.5)	16 (40.0)
>65 Years	8 (6.7)	5 (6.2)	3 (7.5)
Marital Status			
Married	90 (75.0)	58 (72.5)	32 (80.0)
Unmarried	30 (25.0)	22 (27.5)	8 (20.0)
Type of Family			
Nuclear	62 (51.7)	45 (56.2)	17 (42.5)
Joint	58 (48.3)	35 (43.8)	23 (57.5)
Educational Status			
Illiterate	24 (20.0)	14 (17.5)	10 (25.0)
Primary level	40 (33.3)	23 (28.8)	17 (42.5)
Secondary and Above	56 (46.7)	43 (53.8)	13(32.5)
Occupations			
Unemployed	15 (12.5)	9 (11.2)	6 (15.0)
Informal Occupations	28 (23.3)	22 (27.5)	6 (15.0)
Formal Occupations	77 (64.2)	49 (61.2)	28 (70.0)
Main source of Income			
Agriculture	59 (49.2)	41 (51.2)	18 (45.0)
Business	21 (17.5)	13 (16.2)	8 (20.0)
Service	19 (15.8)	15 (18.8)	4 (10.0)
Others	21 (17.5)	11 (13.8)	10 (25.0)

Table 1 showed majority of the respondents of cases (75%) and control (93.8%) followed Hinduism. About three fourth (75%) of the respondents were married. One-fifth (20%) of the respondents were illiterate. More

than one in tenth (12%) respondents was unemployed. About half of respondents (49.2%) were engaged in agriculture.

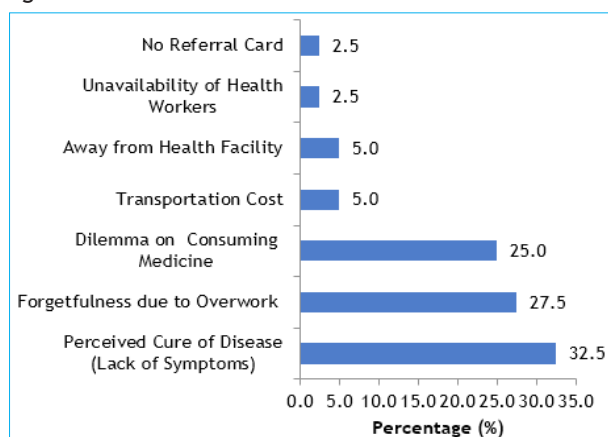


Figure 1. Reasons for Non-Compliance to Tuberculosis Medication.

Figure 1 shows reasons for non-compliance to

tuberculosis medication. About one-third of respondents (32.5%) reported perceived cure of disease followed by forgetfulness due to overwork (27.5%). Very few (2.5%) respondents reported unavailability of health workers in health institution and no referral card as a reason for non-compliance.

Table 2 shows the bivariate analysis of socio-demographic characteristics with tuberculosis treatment compliance. Religion showed the statistically significant association for treatment compliance with unadjusted OR 5.00; CI 1.57-15.85 along with p value 0.006. 75% of the cases and 93.8% of the control followed Hinduism. Similarly, male were found to adhere to medicine significantly as compared to female.

The lifestyle related factors such as previous treatment history, prior use of alcohol and tobacco as well as disease related factors such as presence of diabetes, HIV testing status, knowledge of TB as infectious diseases and high chances of getting HIV infection among TB patients.

Table 2. Association of socio-demographic characteristics of participants.

Characteristics	Compliance	Non- Compliance	P-value	OR	95%CI
Treatment Centre					
Public	72 (90.0)	32 (80.0)		1	
Private	8 (10.0)	8 (20.0)	0.136	2.250	0.776-6.525
Ecological Region					
Terai	33 (41.2)	16 (40.0)		1	0.486-2.283
Hilly	47 (58.8)	24 (60.0)	0.896	1.053	
Gender					
Female	35 (43.8)	11 (27.5)		1	
Male	45 (56.2)	29 (72.5)	0.008*	2.051	0.901-4.668
Age					
>65 Years	5 (6.2)	3 (7.5)		1	
15-40 Years	53 (66.2)	21 (52.5)	0.592	0.660	0.145-3.013
40-65 Years	22 (27.5)	16 (40.0)	0.810	1.212	0.252-5.824
Religion					
Hindu	75 (93.8)	30 (75.0)		1	
Non-Hindu	5 (6.2)	10 (25.0)	0.006*	5.00	1.577-15.854
Marital Status					
Unmarried	22 (27.5)	8 (20.0)	0.373	1	
Married	58 (72.5)	32 (80.0)		1.517	0.606-3.796
Type of Family					
Nuclear	45 (56.2)	17 (42.5)		1	
Joint	35 (43.8)	23 (57.5)	0.157	1.739	0.808-3.745
Educational Status					
Illiterate	14 (17.5)	10 (25.0)		1	
Primary level	23 (28.8)	17 (42.5)	0.094	1.035	0.371-2.885
Secondary and Above	43 (53.8)	13 (32.5)	0.099	0.432	0.152-1.175

Table 3 reveals respondents who had previous treatment history were significantly associated with treatment compliance with unadjusted OR 24.33; CI 8.696-68.087 with p value 0.001. Whereas consumption of alcohol and tobacco in past were not found statistically significant with treatment compliance. Respondents who know about HIV infection is high in tuberculosis patients was found statistical association with unadjusted OR 0.467; CI 0.214-1.016 with medication compliance. 25 (62.5%)

of cases and 35 (43.8%) of control were unknown about HIV infection is high in tuberculosis patients.

Table 4 shows distance of DOTS centers, patients satisfied with waiting time and travelling distance were found to be significantly associated with treatment compliance. Those patients satisfied with waiting time at health facilities were found to have increased chances of consuming TB medication.

Table 3. Association of life style and disease related factors of participants.

Characteristics	Compliance	Non- Compliance	P- value	OR	95%CI
Previous treatment history					
No	73 (91.2)	12 (30.0)		1	
Yes	7 (8.8)	28 (70.0)	0.001*	24.33	8.696-8.087
Alcohol -prior					
No	38 (47.5)	16 (18.0)		1	
Yes	42 (52.5)	24 (60.0)	0.437	1.357	0.628-2.931
Tobacco use Prior					
No	39 (48.8)	18 (45.0)		1	
Yes	41 (51.2)	22 (55.0)	0.698	1.163	0.543-2.490
Presence of Diabetes					
Yes	5 (6.2)	4 (10.0)		1	
No	75 (93.8)	36 (90.0)	0.466	1.667	0.422-6.582
Know about HIV infection is high in tuberculosis patients					
No	35 (43.8)	25 (62.5)		1	
Yes	45 (56.2)	15 (37.5)	0.041*	0.467	0.214-1.016
HIV Testing					
No	44 (55.0)	23 (57.5)		1	
Yes	36 (45.0)	17 (42.5)	0.795	0.903	0.420-1.944
Tuberculosis an Infectious Diseases					
Yes	61 (76.2)	23 (57.5)		1	
No	19 (23.8)	17 (42.5)	0.037	2.373	1.054-5.341

Table 4. Association between accessibility to health care facilities.

Characteristics	Compliance	Non- Compliance	P-value	OR	95%CI
Distance to DOTS Centre (KM)					
≤2	44 (45.0)	7 (17.5)		1	
>2	36 (45.0)	33 (82.5)	0.001*	5.762	2.280-14.559
Use of Vehicle					
Yes	38 (47.5)	14 (35.0)		1	
No	42 (52.5)	26 (65.0)	0.195	1.689	0.767-3.680
Traveling Time(min)					
0-10	20 (25.0)	4 (10.0)		1	
10-30	45 (56.2)	30 (75.0)	0.043	3.333	1.036-10.726
≥30	15 (18.8)	6 (15.0)	0.343	2.000	0.478-8.369
Transportation Cost					

Yes	27 (33.8)	10 (25.0)		1	
No	53 (66.2)	30 (75.0)	0.330	1.528	0.652-3.585
Long duration time for seeking treatment					
No	59 (73.8)	30 (75.0)		1	
Yes	21 (26.2)	10 (25.0)	0.883	0.937	0.392-2.240
Satisfied with Waiting time					
Satisfied	75 (93.8)	33 (82.5)		1	
Dissatisfied	5 (6.2)	7 (17.5)	0.043*	3.182	0.941-10.761
Satisfied with distance travelling					
Satisfied	49 (61.2)	15 (40.0)		1	
Dissatisfied	31 (38.8)	24 (60.0)	0.029*	2.371	1.091-5.153

Table 5. Association between disease perceptions with treatment compliance.

Characteristics	Compliance	Non- Compliance	P-value	OR	95%CI
Tuberculosis Curable by taking the drug regularly					
Yes	77 (96.2)	22(55.0)		1	
No	3 (3.8)	18 (45.0)	0.001*	21.00	5.661-7.898
Importance of medicine in tuberculosis					
No	13 (16.2)	3 (7.5)		1	
Yes	67 (83.8)	37 (92.5)	0.194	2.393	0.641-8.940
Difficulty in explain to other taking medicine					
No	42 (52.5)	22 (55.0)		1	
Yes	38 (47.5)	18 (45.0)	0.796	0.904	0.422-1.937
Stigma					
No	69 (86.2)	33 (82.5)		1	
Yes	11 (13.8)	7 (17.5)	0.588	1.331	0.473-3.744
Attitude of family members on intake of medicine					
Positive	76 (95.0)	33 (82.5)		1	
Negative	4 (5.0)	7 (17.5)	0.035	4.030	1.104-4.709
Satisfied with health service provider's behavior					
Yes	65 (88.8)	31 (77.5)		1	
No	9 (11.2)	9 (22.5)	0.110	2.290	0.829-6.342
Satisfied with counseling					
Satisfied	59 (73.8)	21 (52.5)		1	
Dissatisfied	21 (26.2)	19 (47.5)	0.022	2.542	1.147-5.633
Satisfied with time provided by health workers					
Satisfied	69 (86.2)	25 (62.5)		1	
Dissatisfied	11 (13.8)	15 (37.5)	0.004	3.764	1.526-9.281

Table 5 reveals different statements like tuberculosis is curable by taking drug regularly (OR 21; CI 5.66-77.89), satisfied with counseling (OR 2.54; CI 1.14-5.63), attitude of your family members on regular intake of

medicine (OR 4.03; CI 1.10-14.70), satisfied with time provided by health workers (OR 3.76, CI 1.52-9.28) were found significantly associated with compliance with tuberculosis treatment.

Table 6. Multivariate analysis of factors affecting TB treatment compliance.

Characteristics	Compliance	Non-Compliance	P-value	OR	95%CI	P-value	AOR	95%CI
Previous treatment history								
No	73 (91.2)	12 (30.0)		1			1	
Yes	7 (8.8)	28 (70.0)	0.001*	24.33	8.696-68.087	0.017*	13.455	1.579-114.633
Distance to DOTS Centre (KM)								
≤2	44 (45.0)	7 (17.5)		1			1	
>2	36 (45.0)	33 (82.5)	0.001*	5.762	2.280-14.559	0.021*	4.870	1.272-18.644
Satisfied with Waiting time								
Satisfied	75 (93.8)	33 (82.5)		1			1	
Dissatisfied	5 (6.2)	7 (17.5)	0.043*	3.182	0.941-10.761	0.071	4.655	0.875-24.751
Tuberculosis Curable by taking the drug regularly								
Yes	77 (96.2)	22(55.0)		1			1	
No	3 (3.8)	18 (45.0)	0.001	21.00	5.661-77.898	0.008*	21.633	2.228-210.008
Attitude of your family about regular intake of tuberculosis medicine								
Positive	76 (95.0)	33 (82.5)		1			1	
Negative	4 (5.0)	7 (17.5)	0.035	4.030	1.104-14.709	0.011*	0.094	0.015-0.575
Satisfied with counseling								
Satisfied	59 (73.8)	21 (52.5)		1			1	
Dissatisfied	21 (26.2)	19 (47.5)	0.022	2.542	1.147-5.633	0.174	2.398	0.680-8.455
Satisfied with the time provided by HWs								
Satisfied	69 (86.2)	25 (62.5)		1			1	
Dissatisfied	11 (13.8)	15 (37.5)	0.004	3.764	1.526-9.281	0.209	0.480	0.153-1.510

Table 6 shows adjusted relationship of explanatory variables significant in bivariate analysis with treatment compliance. Previous treatment history (AOR 13.45; CI 1.57-114.63), distance of DOTS centre (AOR 4.870; CI 1.27-18.64), tuberculosis Curable by taking the drug regularly (AOR 21.638; CI 2.22-210.00), attitude of your family about regular intake of tuberculosis medicine (AOR 0.094; CI 0.015-0.575) were significantly associated with treatment compliance.

The qualitative interviews done among the patients and focal persons identified following barriers for TB treatment compliance.

Majority of the participants during FGDs and individual interviews from all six districts stated that because of long distance they were having problems regarding regular medication of tuberculosis. Most of the health service providers were facing difficulties in implementing daily DOTS as people were not able to come to the health facility regularly to take medicines.

“Some wards in our VDC are too far from health facility and it is difficult for us to visit health facility regularly

for medicine”. -(FGD, tuberculosis patient, Tanahun)

“...they have to walk long distance to visit health facility. Elder patients and severe patients cannot come to the health facility regularly to take medicine”. -(In-Depth Interview, Health service provider, Tanahun, Gajarkot)

Majority of the participants shared that the policy of visiting health facility regularly for taking medicine was standing as a barrier for treatment compliance as people felt difficulty in visiting health facility due to work every day for DOTS, especially by weak patients, sick people, elder people and differently able people. Also, few participants reported that people may not even take medicine or leave medication because of the difficulty to visit health facility regularly as people have to do their work as well. Health service providers were found to have problems in implementing DOTS program as people feel difficult to visit health facility every day. Few of the tuberculosis patients during FGDs also revealed that they were getting medicine for some additional days upon request.

“We talk about daily DOTS but it is not possible here. We will be beaten by public if we try to bring all the patients to health facility to consume medicine. We provide medicine to FCHVs or the neighbours of the patients. And we tell them to bring the cover of the medicine to confirm if they took the medicine or not”. -(FGD, Health service provider, Parsa, Srisiya)

Most of the participants reported that they were having problem in regular medication because of poor economic condition. Significant number of participants shared that they were not coming to get medicine because they have to work for living and they were not able to bear every day travel costs or accommodation expenses in order to visit health facility.

One community person said “Government has distributed tuberculosis medicines for free now but travel fare to come and go is Rs.500”. -(FGD, tuberculosis patients, Nawalparasi, Makar

Majority of the health service provider during FGDs and individual interviews from all 6 districts shared that it was difficult for them to convince tuberculosis patient to come to health facility for regular medication.

“We counsel them to take medicine for 6 months but they go for sputum test after 2 months and they themselves look at their report and say that they are cured. So, they stop taking medicine after 2 months. They do not obey to take medicine regularly though we counsel them many times.”-DOTs focal person (Bara & Parsa)

Significant number of participants during FGDs and individual interviews reported that people lack education and awareness about tuberculosis DOTS and necessity of complete medication due to which people do not take medicine regularly and also has resulted in relapse and defaulter cases. Few of the health service providers said that people would not come for final diagnosis or follow up which was also a barrier in detection of cured cases.

“Our community has relapse cases because of lack of awareness about intake of full dose of medicine. Medicines are available but people do not know about taking medicines until they are cured”. -(In-depth interview, Health Service Provider, Tanahun)

“First, they are lacking awareness regarding the treatment of tuberculosis. Due to this, they do not take medicine regularly, they stop taking medicine in the middle because they think that they are cured by taking medicine for 2 months. They do not go for final test

of sputum in order to identify whether they are cured by their full dose of medicine or not.... drug resistance is increasing. In the community, uncured tuberculosis is going to be increased”. -(In-Depth Interview, Public Health Officer, Tanahun)

Some of the participants during FGDs and individual interviews reported that there was greater possibility for people to leave medication because of longer duration of medication and hence increase chances for defaulter.

“Patients feel weak and stressed. They may stop taking medicine thinking that they have already taken medicine for long time but did not get cured.”-(FGD, Tuberculosis patients, Mustang)

“Its treatment schedule is long. In the treatment of other disease, there is medicine for 5 days, patient takes that and gets cured. But in this disease, medicine should be taken for 6 months to 8 or 9 months. This is also a barrier.”-(In-depth interview, Health service provider, Parsa)

Majority of the health service provider during individual interviews reported that patients demand more medicine at a time because they did not want to visit health facility regularly. Most of the participants shared that people give them pressure, apply political powers or powers from people with high profile, threaten and torture them and even behave rudely while asking for more medicines.

“First thing is that patient demand medicine for 1 week, 2 weeks, 10 days or a month. They do phone calls. They use power of leaders and threaten us. They say, “Why do you have to be superior? You may also sometimes have problems. What is problem in providing medicine for a week?” -(In-depth interview, Health Service Provider, Pokhara)

Most of the participants during FGDs and individual interviews shared that there is greater possibility for people to leave medication or loss of patients because of various reasons like longer and regular medication, side-effects, lack of time, economic condition, jobs and lack of awareness and so on and health service provider had to go in search of those patients. Participants reported that people do not come for follow up and stay without taking medicine as they presume that they got cured which resulted in defaulter or relapse cases.

“We have one case here. Category 1 case had come and we kept him here continuously for 10-15 days then he got lost. Again, he came back after 10-20 days and again

got lost... it is difficult for us if such cases come". -(In-depth Interview, Health service provider, Kathmandu, PHC)

Few of the participants from Mustang and Kathmandu during FGDs and in-depth interview reported that patient do not come for regular medication because of their migration. Participants emphasized that people demand medicine as they had to migrate to other place especially for their work.

"There is a Tibetan camp in which different people come to visit and they transmit the disease to one another in the crowd...Migration has resulted problems. People from Gorkha, Dhading and other places migrate here for their daily wages. They demand medicine for a week. When we refuse for medicine then they say that they have to go to upper Mustang to earn daily wages for their morning and evening food". -(In-depth interview, Health service provider, Jharkot, Mustang)

This study showed that patient suffering from tuberculosis are mostly stigmatized, which included fear of isolation, transmission of disease, insult, stigmatized for lifetime and fear of not being accepted that leads to barrier in compliance.

"We have seen that daughter-in-law is compelled to leave the house, students are restricted from the school, and employees are made to leave the office due to tuberculosis. Due to this reason, many people hide tuberculosis and try to take medicine secretly from the health facility". (In-depth interview, Focal person, Kathmandu, DPHO)

Along with this, majority of the participants shared that society and other people would neglect them, dominate them, insult them if they come to know that they have tuberculosis or had any tuberculosis history.

"We have taken medicine and recovered. Still, if we walk outside then people say that s/he has this disease and hate us to some extent. They say "Oh, tuberculosis patient came. We should not stay near to him/her.-(FGD, Tuberculosis patient, Nawalparasi)

DISCUSSION

Tuberculosis treatment compliance is fundamental for successful tuberculosis control and eradication. Compliance to treatment regimens is affected by numerous factors as socioeconomic, health care, therapy related, patient related which need to be explore out and utmost important to addressed those barriers.¹² A

mixed method approach was adopted to explore the barriers in treatment compliance.

Our study found no statistical significant association of treatment compliance with education level which contrasts with the study done in South Ethiopia which shows education is significantly associated (P 0.02) with treatment compliance.¹³ It might be due to differences in literacy level. The present study showed no statistical association of treatment compliance with gender, marital status, ethnicity which corresponds to the findings of the study done in South Ethiopia by Woimo TT et al.^{12,13} Distance of DOTS centre was found statistical association with treatment compliance (p 0.0001, OR 5.762; CI 2.28-14.55). These finding echo with the study that found distance of DOTS center to be a factors associated with treatment compliance.¹³ In qualitative finding, tuberculosis patients expressed visiting health facility regularly for taking medicine was standing as a barrier for treatment compliance as it is difficult to visit health facility every day for daily DOTS, especially by weak patients, sick people, elder people and differently able people.

Travelling time was found statistically associated with the compliance of the treatment (p 0.043) which is in-line with the study of Ethiopia which shows statistical association of treatment compliance with travelling time (p <0.001; OR 3.9; CI 2.1-7.1).¹³ In multiple logistic regression analysis, distance to DOTS center was found statistical association with treatment compliance (AOR 5.76; CI 2.28-14.55) which corresponds with the findings of the study done by Woimo TT. Travelling time, education, occupation weren't found statistically significant with treatment compliance which corresponds to the finding of the study done in Ethiopia.¹³

In the present study, 27.5% respondents reported forgetfulness as reasons for non-compliance of treatment which corresponds with the study done in Ukraine. Stigma and misconception had also affected in the treatment compliance. Tuberculosis patients were stigmatized, which included fear of isolation, transmission of disease, insult, stigmatized for lifetime and fear of not being accepted that leads to barrier in compliance. Similar finding was observed in the study done by Aibana et al. where patients feels stigmatized and rejected by friends and family after disclosing their tuberculosis diagnosis thus started self-treatment.¹⁴

In the study, tuberculosis patients lack education and awareness about tuberculosis DOTS and necessity of full dose of medicine due to which people missed medicine and resulted in relapse and defaulter cases which was

found similar to the study of Ukraine.¹⁴

In the majority of instances, patients' visits at health centre are encountered by lack of staff and the lack of diagnostics. Sometimes, even with the presence of staff, poor communication to patients may lead to the perception of inadequate time with the health workers which can further lead to lack of comprehensibility (of the disease and the prescription), and thus may perpetuate the mistrust and poor compliance. Lack of adequate time and poor attitude by health service providers were major barriers in compliance to the treatment in Pakistan.¹⁵ Together with the incomplete follow-ups and compliance, patients may ultimately develop (multi-drug) resistant tuberculosis.¹⁶

Socio-demographic characteristics of patients are often multi-burdened by their own limitations that include the accessibility to the health centers, economic constraints, patients' awareness and practice of visiting multiple health care providers. These factors are further complicated by the stigma attached to being diagnosed as tuberculosis patients, seeking treatment at the health centre including compliance for a long and complicated tuberculosis regimen.¹⁷

A long and complex regimen of tuberculosis treatment can discourage compliance, particularly when compounded by the patient's condition, accessibility, and economic constraints. A patient may forget, feel exhausted to take the medicine and more importantly may fall prey to the cycle of distance, money and time required for the current DOTS treatment that requires a daily visit to the health centre.^{11,18} The assessment of treatment compliance was based on self-reports of the individual which is liable to recall bias and may under and overestimate patient compliance.

CONCLUSIONS

Wider ranges of barriers are prevalent in context of tuberculosis treatment pathway and outcome. Most importantly, complex and longer treatment regimen complicated by DOTS make it exhausting for health service providers convince patient for adhering optimally to the prescribed regimen. Geographical and economic issues were pronounced barriers to treatment completion reported by both patients and care providers. DOTS playing tremendous role to ensure treatment adherence has itself been identified as major barrier to adherence as well. Enablers of adherence need to be emphasized to address the barriers. Enhancement of community DOTS program is must to made services accessible to patients. Similarly, health service providers should provide proper

counseling about importance of medication on recovery at the time of medication.

ACKNOWLEDGMENTS

We would like to thanks all the research participants who provide their valuable time. We would also like to thanks WHO-TDR, the Special Programme for Research and Training in Tropical Diseases who had finically supported for the research. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. We are grateful to former directors of National Tuberculosis Centres: Dr. Kedar Narsing KC, Dr. Bikash Lamichhane and Dr. Rajendra Pant for the coordination of this study. We would like to thank all District (Public) Health Authorities for the facilitation of the study: Shambhu Prasad Gyawali (Mustang), Sagar Prasad Ghimire (Kaski), Durga Datta Chapagain (Tanahun), Shree Krishna Bhatta (Kathmandu), Jaya Bahadur Karki (Nawalparasi) and Raj Kishor Pandit (Parsa).

Author Affiliations

¹Manmohan Memorial Institute of Health Sciences, Kathmandu, Nepal

²Health Research Together Initiative (HeaRT-Initiatve), Kathmandu, Nepal

³National Academy of Medical Sciences, Kathmandu, Nepal

⁴National Tuberculosis Centre, Ministry of Health and Population, Bhaktapur, Nepal

⁵Krishan Medial and Technical Research Centre, Janakpurdham, Nepal

⁶Liverpool School of Tropical Medicine, Department of Clinical Sciences, Liverpool, UK

⁷Nepal Health Research Council, Kathmandu, Nepal

Competing interests: None declared

REFERENCES

1. WHO. Global tuberculosis report 2020 [Internet]. 2020 [cited 2021 Feb 24]. Available from: <https://www.who.int/publications-detail-redirect/9789240013131>
2. WHO. WHO End TUBERCULOSIS Strategy [Internet]. WHO. World Health Organization; 2015 [cited 2021 Feb 24]. Available from: http://www.who.int/tuberculosis/post2015_strategy/en/
3. Johansson E, Diwan VK, Huong ND, Ahlberg BM. Staff and patient attitudes to tuberculosis and compliance with treatment: an exploratory study in a district in Vietnam.

- Tuber Lung Dis Off J Int Union Tuberc Lung Dis. 1996 Apr;77(2):178–83. [Article]
4. Bawankule S, Quazi SZ, Gaidhane A, Khatib N. Delay in DOTS for new pulmonary tuberculosis patient from rural area of Wardha District, India. *Online J Health Allied Sci* [Internet]. 2010 Jul 30 [cited 2021 Feb 24];9(1). Available from: <http://cogprints.org/6991/> <http://www.ojhas.org/issue33/2010-1-5.htm>
 5. Figueiredo TMRM de, Villa TCS, Scatena LM, Cardozo GR, Isabel R-NA, Nogueira J de A et al. Performance of primary healthcare services in tuberculosis control. *Rev Saúde Pública*. 2009;43(5):825–31. [Article]
 6. Tadesse T, Demiiin-depth interviewee M, Berhane Y, Kebede Y, Abebe M. Long distance travelling and financial burdens discourage tuberculosis DOTs treatment initiation and compliance in Ethiopia: a qualitative study. *BMC Public Health*. 2013 May 1;13:424. [Article]
 7. Chani K. *Factors affecting compliance to tuberculosis treatment in Andara Kavango region Namibia* (Doctoral dissertation). [Article]
 8. Ibrahim LM, Mangveep L, Nguku P, Dankoli R, Waziri NE, Akhimien MO, et al. Factors associated with interruption of treatment among Pulmonary Tuberculosis patients in Plateau State, Nigeria, 2011. 2014;17(78). [Article]
 9. Bam DS, Bam TS, Gunneberg C, Jha K, Pant R. Success story of tuberculosis control in Nepal. *SAARC J Tuberc Lung Dis HIVAIDS*. 2004;1(1). [Article]
 10. Yadav R, Kaphle H, Yadav DrD, Gurung S, Khatri E, Baral S. Factors Associated with Treatment Adherence among Tuberculosis Patients in Gandaki Province of Nepal. *SAARC J Tuberc Lung Dis HIVAIDS*. 2021 Jan 12;XVIII(1). [Article]
 11. Marahatta SB, Yadav RK, Giri D, Lama S, Rijal KR, Mishra SR, et al. Barriers in the access, diagnosis and treatment completion for tuberculosis patients in central and western Nepal: A qualitative study among patients, community members and health care workers. *PLOS ONE*. 2020 Jan 15;15(1) [Article]
 12. Adherence to long-term therapies: evidence for action [Internet]. Geneva: World Health Organization; 2003. Available from: https://www.who.int/chp/knowledge/publications/adherence_report/en/
 13. Woimo TT, Yimer WK, Bati T, Gesesew HA. The prevalence and factors associated for anti-tuberculosis treatment non-adherence among pulmonary tuberculosis patients in public health care facilities in South Ethiopia: a cross-sectional study. *BMC Public Health*. 2017 Mar 20;17(1):269. [Article]
 14. Aibana O, Dauria E, Kiriazova T, Makarenko O, Bachmaha M, Rybak N, et al. Patients' perspectives of tuberculosis treatment challenges and barriers to treatment adherence in Ukraine: a qualitative study. *BMJ Open*. 2020 Feb 2;10(1):e032027. <https://doi.org/10.1136/bmjopen-2019-032027>
 15. Hill PC, Jackson-Sillah D, Donkor SA, Otu J, Adegbola RA, Lienhardt C. Risk factors for pulmonary tuberculosis: a clinic-based case control study in The Gambia. *BMC Public Health*. 2006 Jun 19;6(1):156. [Article]
 16. Tekkel M, Rahu M, Loit HM, Baburin A. Risk factors for pulmonary tuberculosis in Estonia. *Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis*. 2002 Oct;6(10):887–94.
 17. Coker R, McKee M, Atun R, Dimitrova B, Dodonova E, Kuznetsov S, et al. Risk factors for pulmonary tuberculosis in Ruin-depth interviewa: case-control study. *BMJ*. 2006 Jan 14;332(7533):85–7. [Article]
 18. Dias AAL, de Oliveira DMF, Turato ER, de Figueiredo RM. Life experiences of patients who have completed tuberculosis treatment: a qualitative investigation in southeast Brazil. *BMC Public Health*. 2013 Jun 19;13(1):595. [Article]