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**Correspondence:**

Mr. Sumit KC

Master in Public Health, Public Health Inspector, Nepalgunj Submetropolitan City Office, Nepalgunj, Banke, Nepal

Email: kcsumit38@gmail.com

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## Prevalence of and factors associated with tuberculosis medication adherence among pulmonary tuberculosis patients registered in the DOTS program in Banke district, Nepal

Sumit KC<sup>1</sup>, Srijana Bhattarai<sup>2</sup>, Kabita Khatiwada<sup>3</sup>, Shalabh Shah<sup>4</sup>, Samjhana Sapkota<sup>5</sup>

<sup>1</sup>Master in Public Health (MPH), Public Health Inspector, Nepalgunj Submetropolitan City Office, Banke; Nepal; <sup>2</sup>MPH, Ethnographic Researcher, <sup>4</sup>MPH, Monitoring and Data Analyst, Herd International, Bhaisepati, Lalitpur, Nepal; <sup>3</sup>MPH, Lecturer, Department of Public Health, Modern Technical College, Sanepa, Lalitpur, Nepal; <sup>5</sup>Bachelor in Nursing Science, Staff Nurse, Nepalgunj Submetropolitan City Office, Banke, Nepal

### Abstract

**Introduction:** Tuberculosis (TB) remains a major public health challenge worldwide. Non-adherence to treatment among TB patients threatens control efforts. This study aimed to assess the prevalence of and identify factors associated with medication adherence for pulmonary tuberculosis (PTB) among patients registered under the Directly Observed Treatment Program (DOTS) in Banke District, Lumbini Province, Nepal.

**Method:** A community-based cross-sectional study was conducted among 385 patients with PTB, using stratified and random sampling, and data were collected via telephone interviews. Descriptive and inferential analyses were used. Logistic regression was performed, and p-values less than 0.25 in the bivariate analysis were considered for inclusion in the multivariate logistic regression analysis. Data analysis was done using STATA v13.

**Result:** The prevalence of PTB adherence was 95.58% (95% CI 92.9%-97.2%). Factors significantly associated with adherence included knowledge about TB, walking distance to DOTS centers, waiting time at DOTS centers, and whether health education was provided. Patients with poor knowledge, longer travel or wait times, and those who did not receive health education were significantly less likely to adhere to treatment.

**Conclusion:** However, the prevalence of PTB adherence was 95.58%. Interventions to improve knowledge, reduce access barriers, and provide health education are recommended to achieve 100% adherence. Programs aimed to emphasize the establishment and expansion of community-based DOTS programs and address existing barriers to 100% adherence to the treatment.

**Keywords:** PTB; DOTS; PTB Adherence

## INTRODUCTION

Tuberculosis (TB) is a contagious disease caused by the bacillus *Mycobacterium tuberculosis*, primarily affecting the lungs, also known as pulmonary tuberculosis (PTB). The disease mainly spreads through droplets, and close contact with individuals in the active stage of the disease increases the risk of transmission by approximately 2.5 times.<sup>1</sup> Despite being a well-known illness for over a century and the availability of effective drugs and vaccines, it remains a significant public health concern.<sup>2</sup> In 1993, the World Health Organization (WHO) declared TB a global health emergency, recognizing it as a leading cause of adult mortality.<sup>3</sup> In response, WHO introduced the Directly Observed Treatment, Short Course (DOTS), international strategy in 1994 to reduce TB-related morbidity, mortality, and transmission until TB no longer poses a public health threat.<sup>4</sup> This approach promotes standardized treatment regimens and supervised drug intake to ensure better outcomes.<sup>4</sup>

Sustainable Development Goal (SDG) Target 3.3 aims to end the TB epidemic by 2030. The WHO End TB Strategy defines milestones (for 2020 and 2025) and targets (for 2030 and 2035) to reduce TB cases and deaths.<sup>5</sup> Government of Nepal also follows the path of ending the TB epidemic by 2030. Given priority by the SDGs, WHO, and the Government of Nepal, reducing TB cases is essential to adhering to the TB treatment regimen, thereby decreasing the PTB caseload, including drug-resistant cases, and preventing further transmission.<sup>6</sup>

Adherence to TB treatment, as defined by the WHO, refers to the extent to which a patient's medication-taking coincides with the prescribed treatment regimen.<sup>3</sup> However, TB continues to spread worldwide despite the DOTS strategy.<sup>3</sup> In 2018, an estimated 10 million people contracted TB globally, with the burden ranging from fewer than five to over 500 new cases per 100,000 population annually.<sup>6</sup> The highest cases were reported in the WHO regions of South-East Asia (44%), Africa (24%), and the Western Pacific (18%).<sup>5</sup> In Nepal, about 117,000 people live with TB, with a prevalence of 416 per 100,000 in 2018.<sup>6</sup> Treatment adherence remains crucial, as studies in Ethiopia, India, China, and Kosovo and Nepal have shown varying levels of PTB medication compliance and adherence, directly impacting disease control efforts as 61.4%, 88%, 34.64%, and 85.5% respectively.<sup>7-11</sup> TB medication non-adherence increases the risk of TB transmission, causes drug resistance, and increases morbidity and mortality.<sup>10</sup>

The current anti-TB therapies are challenged with different problems, mainly because of the long-term treatment and the increasing occurrence of medication resistance, which is most likely due to treatment non-adherence and lost to follow-up.<sup>6</sup> Thus, this study aimed to assess the prevalence of and identify factors associated with medication adherence for PTB among patients registered under the DOTS in Banke District, Lumbini Province, Nepal.

## METHOD

A descriptive cross-sectional study with a quantitative approach was conducted to determine the prevalence of PTB medication adherence and the factors associated with it. Data were collected via telephone interviews from a sample drawn across 8 DOTS centers in the Banke district of Lumbini Province, Nepal, where patients were registered under the DOTS program. The duration of this study was six months.

For sample size, prevalence of adherence to pulmonary tuberculosis treatment  $p = 61.4\%$ <sup>11</sup>

Where,

$$p = 0.614$$

$$q = 0.386$$

Z = the standard normal variate, value of Z at 95% confidence interval = 1.96

Non-response rate = 0.1

d = permissible error, value of  $d = \pm 0.05$

Confidence interval = 95%

$$\begin{aligned} \text{Then the estimated sample size (no)} &= (z \times 2 \times p \times q / dx^2) \\ &= \{(1.96 \times 2 \times 0.614 \times 0.386) / 0.05 \times 2\} \\ &= 364.18 \end{aligned}$$

Adding non-response

$$= 364.18 \times (1 + 0.1)$$

$$= 400.6 \sim 401$$

The study sample size was 401. Of the 401 respondents, 385 were enrolled in the study, and the remaining 16 were non-responders. In this study, all PTB patients registered for PTB treatment at DOTS centers in Banke District who provided informed consent via telephone participated.

A stratified proportionate sampling method was used. The local government bodies were considered as strata (i.e., a total of eight strata). A proportional allocation was made for the required number of samples from each stratum. In each stratum, simple random sampling was used to select patients registered in the DOTS program. To choose the respondent, a random number method was used using Microsoft Excel version 2016.

The data were collected through telephone interviews, and the questionnaire was adapted from a study on "compliance with DOTS among tuberculosis patients under community-based DOTS strategy done in Palpa district, Nepal".<sup>11</sup> The questionnaire consisted of five parts- the first part was used to collect socio-demographic information of the respondents, the second part was used to gather knowledge about tuberculosis, the third part was used to collect information related to accessibility to DOTS services, the fourth part was used to collect information related to the availability of DOTS services and fifth part was used for assessing the medication adherence. Approval for the study was obtained from the IRC-PAHS (Reference Number: PHP2009151446) and also from the local government body of Banke district. Informed consent was obtained through

a telephone interview and recorded separately for each respondent. The study included all PTB patients registered for PTB treatment at DOTS centers in the Banke district who provided informed consent via telephone. Others who did not meet the criteria were excluded.

The collected data were coded, entered, and cleaned using Epi-Info version 7. Data were analyzed using STATA software version 13. The normalized weight was used in computing the weighted frequency distribution of the variables to adjust the samples for the weighted total after correcting it for non-response errors.

The descriptive statistics, including percentages and frequency distributions, were computed for background variables, knowledge about tuberculosis, the availability of DOTS services, and access to DOTS services. Bivariate and multivariate logistic regression analyses were conducted to investigate the relationship between the dependent and independent variables. A variance inflation factor (VIF) value of less than two was used to determine the final model.

## RESULT

The finding revealed that respondents were aged 18–77 years, with a median age of 40 years. The majority (88.2%) identified as Hindu, and nearly half (49.7%) were of Brahmin or Chhetri ethnicity. Almost all respondents (98.7%) were literate, with 50.3% having attained secondary-level education. Additionally, a large portion of respondents (74.5%) were unemployed and identified as homemakers. The number of female respondents with pulmonary tuberculosis was lower than that of males, i.e., 173 (44.94%) and 212 (55.06%), respectively. Regarding the respondents' occupations, 123 (31.95%) were involved in agriculture, 46 (11.95%) in labor, 51 (13.25%) as housemakers, 22 (5.71%) as business owners, and 86 (22.34%) were unemployed. Regarding respondents' educational level, 21 (5.45%) were illiterate, and 123 (31.95%) had higher secondary (11-12 class) or higher educational levels. Similarly, the respondents' marital status: 267 (69.35%) were married, and 3 (0.78%) were separated. Almost 365 (94%) of respondents had a high monthly family income, and three (0.78%) had a low monthly family income.

The study found that the prevalence of PTB medication adherence among PTB respondents was 368 (95.58%), and of non-adherence was 17 (4.42%).

The study found that PTB respondents' knowledge of PTB medication adherence was good: 345 (89.61%) had good knowledge, and 40 (10.39%) had poor knowledge.

Study found that more than 340 (88.31%) respondents had travel costs of less than or equal to 10 Nepali rupees as travel costs to the nearby DOTS center, and the remaining 45 (11.69%) respondents had to pay more than 10 Nepali rupees as travel costs to reach the DOTS center for PTB drugs. Walking distance from the DOTS center showed that 359 (93.25%) respondents required less than or equal to

**Table 1. Socio-demographic Information**

Variables	Unweighted	Weighted
	f (%) (n = 385)	f (%) (n = 385)
Age		
15-34	118(30.65%)	118.04(30.62%)
35-54	183(47.53%)	183.68(47.65%)
≥ 55	84(21.82%)	83.72(21.72%)
Gender		
Male	215(55.06%)	212.27(55.06%)
Female	170(44.94%)	172.17(44.94%)
Occupation		
Agriculture	123(31.95%)	123.59(32.06%)
Labor	46(11.95%)	46.15(11.97%)
Housemaker	51(13.25%)	50.86(13.20%)
Service/job	57(14.81%)	56.81(14.74%)
Business	22(5.71%)	21.76(5.65%)
Unemployed	86(22.34%)	86.27(22.38%)
Education level		
Illiterate	21(5.45%)	21.07(5.47%)
No formal schooling	79 (20.52%)	78.8(20.45%)
Primary school(1-5 class)	107(27.79%)	107.39(27.86%)
Secondary(6-10 class)	55(14.29%)	55.21(14.32%)
Higher secondary(11-12 class) and above	123(31.95%)	122.96(31.90%)
Marital status		
Never married	78(20.26%)	77.96(20.23%)
Married	267(69.35%)	267.67(69.45%)
Separated	3(0.78%)	2.91(0.75%)
Widow/ Widower	37(9.61%)	36.9(9.57%)
Monthly family income (NRs)		
Low income (<2500)	3(0.78%)	2.97(0.77%)
Middle income (2500-5000)	17(4.42%)	16.97(4.40%)
High income (> 5000)	365(94.81%)	365.5(94.83%)

**Table 2. Prevalence of PTB medication adherence**

PTB medication adherence	Unweighted	Weighted
	f (%)	f (%)
Yes	368(95.58%)	368.66(95.65%)
No	17(4.42%)	16.78(4.35%)

**Table 3. Knowledge of PTB patients**

Knowledge about PTB	Unweighted	Weighted
	f (%)	f (%)
Good knowledge	345(89.61%)	346.13(89.80%)
Poor knowledge	40(10.39%)	39.31(10.20%)

30 minutes to travel to the DOTS center for PTB drugs, and the remaining 26 (6.75%) required more than 30 minutes. Waiting time at the DOTS center was normal (<15 minutes) for 365 (94.81%) respondents, and the remaining 20 (5.19%) respondents reported a long waiting time (≥15 minutes). Similarly, a health worker (PTB focal person) was available in 377 (97.92%) respondents' visits, and the remaining eight (2.08%) respondents didn't find a health worker (TB focal person) during their visit to the DOTS center for PTB drugs. Health education and PTB medications were received by 257 (66.75%) respondents, while the remaining 128 (33.25%) received only tuberculosis medications during their visit to the DOTS center. All respondents (100%) received PTB

**Table 4. Bivariate analysis of mediating variables and PTB medication adherence**

Variables	PTB medication adherence		Unadjusted analysis OR (95% CI)	p-value
	Yes	No		
Knowledge about pulmonary tuberculosis				
Good knowledge	337(97.68%)	8(2.32%)	1	
Poor knowledge	31(77.50%)	9(22.50%)	0.08(0.02-0.22)	<0.25*
Accessibility of DOTS service				
Travel cost				
Less than and equal to 10 NRs	330(97%) (97.06%)	10(2.94%)	1	
More than 10 NRs	38(84.44%)	7(15.56%)	0.16(0.05- 0.45)	<0.25*
Distance from DOTS center				
Less than and equal to 30 minutes	352(98.05%)	7(1.95%)	1	
More than 30 minutes	16(61.54%)	10(38.46%)	0.03(0.01-0.09)	<0.25*
Waiting time				
Normal waiting time(<15minute)	354(96.99%)	11(3.01%)	1	
High waiting time(≥ 15 minute)	14(70%)	6(30%)	0.072(0.02-0.22)	<0.251*
Availability of DOTS service				
Availability of health worker				
Yes	361(95.76%)	16(4.24%)	3.22(2.37-0.80)	0.3508
No	7(87.50%)	1(12.50%)	1	
Health education by the health worker				
Health education and TB drug	254(98.83%)	3(1.17%)	1	
TB drug only	114(89.06%)	14(10.94%)	0.096(0.02-0.34)	<0.25*

**Table 5. Multivariate analysis of mediating variables and PTB medication adherence**

Variables	AOR	95% CI	p-value
Knowledge			
Good knowledge	1		
Poor knowledge	0.18	0.04 – 0.78	<0.05*
Travel cost			
Less than and equal to 10 NRS	1		
More than 10 NRS	0.4	0.23 – 7.37	0.76
Walking distance			
Less than and equal to 30 minutes	1		
More than 30 minutes	0.016	0.002 - 0.09	<0.05*
Waiting time			
Normal waiting time	1		
High waiting time	0.0692	0.01 – 0.34	<0.05*
Service at DOTS center			
Health education and PTB drug	1		
PTB drug	0.1	0.02- 0.51	<0.05*

medications at the DOTS center.

The multivariate analysis is done by controlling for other independent variables. When these three variables were analyzed, the p-values for the occupation and education level variables were significant ( $p < 0.05$ ). After obtaining a significant p-value, multicollinearity was checked using VIF, which yielded a value greater than 2, indicating multicollinearity among the independent variables. Multivariate analysis was performed to examine the relationship between the mediating variables and the dependent variable. The analysis showed that all variables were significant, with p-values less than 0.05, except travel cost.

A final multivariate logistic regression was performed, including knowledge of PTB, walking distance to the DOTS center, waiting time at the DOTS center, and health education by the health worker. These mediating variables

**Table 6. Final model analysis of independent variables and PTB medication adherence**

Variables	AOR	95% CI	p-value
Knowledge of TB			
Good knowledge(ref.)	1		
Poor knowledge	0.191	0.04 - 0.79	< 0.05*
Distance from DOTS center			
Less than and equal to 30 minutes(ref.)	1		
more than 30 minutes	0.018	0.003 - 0.08	< 0.01*
Waiting time			
Normal waiting time(ref.)	1		
High waiting time	0.0719	0.014 – 0.346	<0.05*
Health education by the health worker			
Health education and PTB drug(ref.)	1		
PTB drug	0.1	0.02 - 0.50	< 0.01*

were retained in the final multivariate model because their p-values were <0.05. After computing VIFs, these variables had VIFs below 2, indicating no multicollinearity among the independent variables, so they were kept in the final model and further interpreted.

PTB patients with poor knowledge had an odds ratio of 0.191 (95% CI 0.04 - 0.79) for PTB medication adherence compared to those with good knowledge about PTB. PTB patients whose walking distance to the DOTS center on foot was more than 30 minutes had an odds ratio of 0.018 (95% CI 0.003 - 0.08) for PTB medication adherence, compared with those with a walking distance of 30 minutes or less.

Similarly, PTB patients who had to wait more than 15 minutes in the DOTS center during office days and hours had an odds ratio of 0.0719 (95% CI 0.014 - 0.346) times for PTB medication adherence as compared to those who

had to wait for less than or equal to 15 minutes in the DOTS center during office days and hours. Those PTB patients who received only TB drug during their visit to the DOTS center had an odds ratio of 0.10 (95% CI 0.02 – 0.50) for PTB medication adherence, compared to those who received health education and TB drug during their visit to the DOTS center.

## DISCUSSION

The present study revealed that the prevalence of PTB medication adherence was 95.58% (95% CI 92.9–97.2). This is higher than the previous study of Nepal (61.4%, 74.7%).<sup>11,12</sup> A similar study conducted in India showed that the percentage of PTB patients who had adhered to treatment was 88.18%.<sup>13</sup> A study done in Nigeria showed that 70.3%,<sup>14</sup> Iran indicated that 92%.<sup>15</sup>

The present study assessed knowledge of, access to, and availability of DOTS services. No significant relationship was observed with socio-demographic variables.

This study found that PTB patients with poor knowledge had an odds ratio of 0.191 (95% CI 0.04 - 0.79) for PTB medication adherence compared to those with good knowledge about PTB. A similar result was shown by a study conducted in Kailali, Nepal (p-value <0.001).<sup>16</sup> A study in Indonesia showed that knowledge of respondents was directly related to PTB medication adherence (p-value less than 0.05).<sup>17</sup>

These results were comparable to those from a study in Ethiopia, which found that respondents with good knowledge were 5.5 (95% CI 0.94–30.7) times more likely to adhere to treatment than those with poor knowledge.<sup>7</sup>

A study in Nigeria showed that knowledge about TB is important for PTB adherence, i.e., (AOR 6.1; CI 95%: 2.8–13.2).<sup>14</sup> These results from the different studies showed that knowledge is an important factor for PTB adherence.

This study presented that PTB patients whose walking distance from the DOTS center on foot was more than 30 minutes had an odds ratio of 0.018 (95% CI 0.003 - 0.08) times for PTB medication adherence as compared to those who had less than or equal to 30 minutes of travel distance from the DOTS center on foot. Another study from Kailali and Palpa, Nepal, supported this finding (p-value <0.001).<sup>16,11</sup>

A study conducted in Oman showed that walking distance was directly related to PTB medication adherence (p-value <0.005).<sup>18</sup> Similarly, another study done in China reported that more walking time was more likely to lead to non-adherence by 1.41 times (95% CI 1.04–1.92).<sup>8</sup> This result was different but comparable with a study done in Ethiopia, which showed that respondents' walking distance was directly related to PTB medication adherence (AOR 21.830; 95% CI = 0.054–77.500).<sup>1</sup>

This study showed that PTB patients who had to wait more than 15 minutes in the DOTS center during office days and

hours had an odds ratio of 0.0719 (95% CI 0.014 - 0.346) times for PTB medication adherence as compared to those who had to wait for less than and equal to 15 minutes in the DOTS center during office days and hours. A similar result was shown by a study done in Ethiopia, which described that patients with high waiting time in the DOTS center had (AOR 14, 95% CI 2.135, 95.241) a higher chance of non-adherence than with normal waiting time.<sup>1</sup> Another supporting study done in South Ethiopia showed that patient waiting time was directly related to PTB adherence (AOR 1.022, 95% CI 1.009–1.0035).<sup>19</sup>

This study revealed that respondents who only got the PTB drug during their visit to the DOTS center had an odds ratio of 0.10 (95% CI 0.02 – 0.50) times for PTB medication adherence as compared to those who got health education and the PTB drug during their visit to the DOTS center. A study done in Kathmandu, Nepal, showed that patients getting health education at every visit were adherent to treatment by 6.27 times (95% CI 2.88–13.64 ) compared to non-adherent.<sup>12</sup> Studies done in Palpa, Nepal, showed that health education from a treatment supervisor in every visit accounted for the increase in patients' adherence to the treatment (p=0.02).<sup>11</sup> Furthermore, another study done in Bangladesh showed that health education was directly related to PTB adherence with a p-value less than 0.05.<sup>20</sup>

## CONCLUSION

The study concludes that PTB patients with poor knowledge were 0.191 times (95% CI: 0.04–0.79) less likely to adhere to medication, those walking more than 30 minutes to a DOTS center were 0.018 times (95% CI: 0.003–0.08) less likely to adhere, and those waiting more than 15 minutes were 0.0719 times (95% CI: 0.014–0.346) less likely to adhere. Similarly, patients who only received TB drugs without health education were 0.10 times (95% CI: 0.02–0.50) less likely to adhere to medication, indicating that better knowledge, shorter distance, reduced waiting time, and effective health education significantly improve PTB medication adherence.

The study recommended that health institutions should be directed to increase the knowledge of patients regarding PTB. Priority should be given to PTB patients, when they visit the DOTS center, to decrease the waiting time of PTB patients. Health education and information related to PTB should be given to PTB patients by health workers during each visit of the patients to the DOTS center. Establishment and expansion of community-based DOTS program to decrease travel time of the patients to DOTS centers are recommended for 100% adherence to the treatment and contributing to the target of sustainable goal for 2030.

## DECLARATIONS

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### Conflict of Interest

The author declares no conflict of interest with others regarding this research work.

### Funding

None

### Ethical Clearance

Approval for the study was obtained from the IRC-PAHS (Reference Number: PHP2009151446) and also from the local government body of Banke district.

### Consent for the Study

Informed consent was obtained through a telephone interview and recorded separately for each respondent.

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