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Original Investigation

Adherence to Anti-tubercular Agents in DOTS Center in Western Nepal

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ABSTRACT

INTRODUCTION: Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis and is one of the major public health problems in developing countries like Nepal. Despite the availability of effective tuberculosis treatment regimens, patients must take a combination of anti-tubercular drugs for at least six months and may endure numerous side effects, making treatment compliance exceedingly difficult to maintain. The primary objective of the study was to assess the adherence rate to anti-tubercular agents and to find the prevalence of adverse drug reactions to the anti-tubercular therapy. **MATERIALS AND METHODS:** This study was an observational study conducted in the DOTS centers of UCMS-TH, Bhairahawa, and Lumbini Provincial Hospital Butwal. A semi-structured questionnaire was used to collect data from 170 participants to determine the adherence rate to anti-tubercular therapy and the incidence of associated adverse drug reactions. Statistical Package for Social Sciences (SPSS Version 20) program was used to enter and analyze the data. The association between adherence and other variables was established using the Chi-square test. **RESULTS** The adherence rate to anti-tubercular therapy was found to be 159 (93.5%). The major reasons for non-adherence include forgetfulness 8 (72.72%) followed by adverse effects 2 (18.18%) and transport difficulty in reaching the health facility 1 (9.1%). The prevalence of adverse drug reactions was 58 (34.12%) (27.1 - 41.2 at 95% Confidence Interval). Adherence was significantly associated with the experience of adverse effects, literacy, marital status, area of residence, and age of the participants. **CONCLUSIONS:** The adherence rate to anti-tubercular therapy was very high, which can be the primary determinant of tuberculosis treatment success.

Keywords: Adherence, anti-tubercular agents, prevalence, tuberculosis.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis and is one of the biggest public health issues in developing countries like Nepal. The estimated prevalence of TB patients in Nepal is around 375 patients in 1 lakh population [1]. Through Directly Observed Treatment Short course (DOTS) treatment centers and sub-centers, the Ministry of Health and Population (MOHP) of Nepal offers free TB treatment to all patients. Despite the availability of efficient TB treatment regimens, maintaining adherence to the treatment regimen may be difficult as TB patients must take a combination of anti-tubercular medications for an extended period of at least six months [2]. Treatment adherence is a major factor in TB treatment success and TB patient's quality of life [3]. DOTS technique requires patients to visit a TB treatment facility each day for at least the first two months of the intensive phase to observe treatment in person. One of the main causes of the development of drug-resistant Mycobacterium tuberculosis strains and consequent treatment failure is non-adherence [4]. Socioeconomic status, the effectiveness of the healthcare system, social support, drug side effects, and contact with medical staff are some additional characteristics that have

been connected to non-adherence to TB treatment [5, 6]. The present study's primary objective was to determine the adherence rate to anti-tubercular therapy (ATT) / anti-tubercular agents in the DOTS center of western Nepal and the prevalence of adverse drug reactions in the participants. The findings of this study may assist MOHP in identifying viable strategies for improving patient adherence to TB treatment regimens.

MATERIALS AND METHODS

Study design and setting

This cross-sectional study was carried out in the DOTS centers of UCMS-TH, Ranigaun, Bhairahawa, and Lumbini Provincial Hospital Butwal, starting from February 2022 to May 2022 for four months duration.

Participants, sample size and sampling technique

All the TB patients who were above 15 years of age, registered under DOTS therapy, and those who completed at least 30 days under DOTS medication were included in this study. Those patients who disagreed with consent, severely ill and mentally ill, were excluded.

Purposive sampling technique was used in this study. The sample size was calculated using Cochran's formula, taking the success rate of tuberculosis as 89% [7] (National Tuberculosis Centre, 2019) with a confidence level of 95% and a degree of precision of 5%. Sample Size (N) = z^2 p q / d^2 = $(1.96)^2$ x 0.89 x 0.11 / $(0.05)^2$ = 150.43 .Where, Prevalence (p) = 0.89, q = 1-p= 1-0.89=0.11. Desired confidence level at 95% (z) = 1.96 (For the level of confidence of 95%, which is conventional z value is 1.96). Degree of Precision (d) = 5 % (0.05). The overall computed sample size was roughly 165.47 after accounting for the non-response rate, which was added at 10%. However, 170 participants in total were included in the study.

Data collection procedure and study variables

Data was collected in a structured format using a semi-structured questionnaire and face-to-face interviews with participants and participant's parties. Patients were questioned regarding their compliance with the DOTS regimen and experience of adverse effects during ATT. The rate of medication adherence of TB patients toward ATT was measured using the Morisky Medication Adherence Scale-8 (MMAS-8) [8]. Cross-check questions were adapted to increase the reliability of the study. The questionnaire was written in English and translated into the patient's native tongue according to their needs. To ensure external validity, relevant literature search and expert opinion were considered throughout the study.

Statistical analysis and data management

The Statistical Package for Social Sciences (SPSS) version 20 was used to code and enter the data. The demographic information, adherence rate, reasons for non-adherence, prevalence of adverse drug reactions, and types of ADR experienced were all summarized using descriptive statistics such as frequencies and percentages. The correlation between ATT adherence and related variables was assessed using a chi-square test. P-value of less than 0.05 was considered statistically significant.

Ethical considerations

Ethical approval was taken from Institutional Review Committee of UCMS-TH (UCMS-IRC), Bhairahawa, with approval number (UCMS/IRC/026/22). Verbal and written consent was taken from the participants before each interview, and the research objectives were clarified.

RESULTS

Out of 170 participants, 120 (70.6%) were men, and 50 (29.5%) were women. The age group of 21 to 40 years had the highest percentage of participation, 61 (35.9%). The mean standard deviation for age was 40.61 ± 19.60 years. A total of 56 (32.9%) participants were in the intensive phase of the treatment, whereas 114 (67.1%) participants were in the continuation phase, while 60 (35.3%) patients had TB symptoms (Table 1). Of the participants, 159 (93.5%) were adherent, while the remaining 11 (6.5%) were non-adherent to the DOTS regimen, as shown in Table 2.

The major reasons for non-adherence were found to be forgetfulness 8 (72.7%), adverse effects 2 (18.2%), and transport difficulty 1 (9.1%), respectively. The prevalence of adverse drug reaction was 58 (34.1%) (27.1-41.2 at 95% Confidence Interval). Most frequent ADRs identified during the study included urine discoloration 42 (24.7%), hepatotoxicity 39 (22.9%),

neuropathy 30 (17.6%), and gastric discomfort 18(10.6%) (Table 3). Adherence of the participants to the DOTS regimen was significantly associated with literacy (p<0.001), area of residency (p=0.001), marital status (p=0.029), age (p=0.001), and experience of ADRs (p<0.001), as shown in Table 4.

Table 1| Characteristics of participants (n=170)

Variables	Frequency (%)
Age group (years)	
Below 20	34 (20%)
21-40	61 (35.9%)
41-60	43 (25.3%)
Above 60	32 (18.8%)
(Mean ± Standard Deviation = 40.61 ± 19.60)	
Sex	
Male	120 (70.6%)
Female	50 (29.4%)
Marital status	
Married	121 (71.2%)
Unmarried	49 (28.8%)
Literacy	
Literate	141 (82.9%)
Illiterate	29 (17.1%)
Residence	
Rural	84 (49.4%)
Urban	86 (50.6%)
Phase of therapy	
Intensive	56 (32.9%)
Continuation	114 (67.1%)
TB symptoms	
Present	60 (35.3%)
Absent	110 (64.7%)

Table 2| Adherence of the participants to DOTS regimen (n=170)

Variables	Frequency (%)
Degree of Adherence	
Non-adherent	11 (6.5%)
Adherent	159 (93.5%)
Reason for Non-Adherence (n=11)	
Forgetfulness	8 (72.7%)
Adverse effects	2 (18.2%)
Transport difficulty	1 (9.1%)

Table 3| Prevalence of adverse drug reactions and its types (n=170)

Variables	Frequency (%)
Experience of ADR	
Yes	58 (34.1%)
No	112 (65.88%)
Types of ADR experienced (n=58), Multiple response	
Urine Discoloration	42 (24.7%)
Hepatotoxicity	39 (22.9%)
Neuropathy	30 (17.6%)
Gastric Discomfort	18 (10.6%)
Skin Allergy	15 (8.8%)
Loss of Appetite	6 (3.5%)

Table 4| Association between Adherence to ATT and other variables (n=170).

Variables	Adherence		P-value
	Adherent	Non-Adherent	
Literacy			
Literate	139 (98.6%)	2 (1.4%)	<0.001*
Illiterate	20 (69%)	9 (31%)	
Area of residence			
Rural	73 (86.9%)	11 (13.1%)	0.001*
Urban	86 (100%)	0 (0%)	
Sex			
Male	112 (93.3%)	8 (6.7%)	0.872
Female	47 (94%)	3 (6%)	
Marital Status			
Married	110 (90.9%)	11 (9.1%)	0.029*
Unmarried	49 (100%)	0(0%)	
Age			
Below 20	34 (100%)	0(0%)	0.001*
21-40	60 (98.4%)	1 (1.6%)	
41-60	40 (93%)	3 (7%)	
Above 60	25 (78.1%)	7 (21.9%)	
Phase of therapy			
Intensive	54 (96.4%)	2 (3.6%)	0.282
Continuation	105 (92.1%)	9 (7.9%)	
TB Symptoms			
Present	58 (96.7%)	2 (3.3%)	0.219
Absent	101 (91.8%)	9 (8.2%)	
Experience of ADRs			
Yes	48 (82.8%)	10 (17.2%)	<0.001*
No	111 (99.1%)	1 (0.9%)	

**Statistically Significant, p<0.05*

DISCUSSION

The primary predictor of the success of the TB treatment is adherence to the DOTS regimen. The present study comprised a total of 170 TB patients, out of which 159 (93.5%) adhered to the DOTS regimen while the remaining 11 (6.5%) were non-adherent. The result is consistent with the studies conducted in Ethiopia and Tanzania, where the overall adherence rate to anti-TB treatment was 90.6% and 95.7%, respectively [9,10]. The most plausible explanation for the similarity of the result

is that participant's knowledge, literacy, health care accessibility, and awareness about the consequences of non-adherence to the anti-TB treatment regimen might be the same. In this study, the adherence rate was higher compared to the studies done in Egypt (65.1%), Uganda (75%), Southern Ethiopia (79.2%), India (84%), and Nepal (79.4%) [11-15]. This may be the result of different assessment times, adherence measurement instruments, sample methodologies, and participants growing knowledge and awareness of the effects of non-adherence to anti-TB medication in developing nations.

Forgetfulness 8 (72.70%) was the major reason for non-adherence in the current study, followed by the experience of adverse effects 2 (18.20%) and transport difficulty to DOTS center 1(9.10%), which was similar to studies in Ethiopia [16] and Nigeria [17], and thus highlights the need for more patient education and counseling for significant medication adherence. Inadequate therapy for TB is one of the main reasons for treatment failure and the development of acquired drug resistance [18].

The gender of the participants in this study did not significantly affect adherence, in contrast to a study carried out in Turkey, which found that females were more likely to stick to the recommended regimen than males [19]. This difference might be due to a higher proportion of male (70.6%) participants in our study than their counterparts. The small sample size could be blamed on the inability to detect a relationship between gender and adherence.

The results of the current study revealed a statistically significant relationship ($p=0.029$) between participants marital status and adherence. Contrary to a study from Nanjing, China, which found no significant correlation between adherence and marital status ($p=0.877$) [20], the present study demonstrated that a higher percentage of the unmarried participants were more ATT regimen adherent than the married participants. The difference could be attributed to the fact that the unmarried participants of our study were more literate, informed, and well educated.

The age of the participants in the present study was found to be significantly associated with the adherence to the ATT regimen ($p=0.001$), which is parallel to a study done in Turkey [19]. The participants in the age group 21-40 years and 41-60 years were more adherents than those below 20 and above 60. On the contrary, in a study by Ormerod and Prescott, better adherence was observed in those over 60 years and the worst in young adults aged 15-29. They concluded that the better adherence by older participants might be due to their perception of the seriousness of the diagnosis [21]. Non-adherence in older participants in the present study may be due to the poor level of education in the majority of the participants.

Our study showed a statistically significant relationship between the adherence with the literacy or knowledge of the participants ($p<0.001$), similar to a study conducted in Uganda [12]. A study in the eastern Terai region of Nepal also showed a significant relationship between adherence and the literacy or knowledge of the participants [22]. This result may be due to the higher proportion of literate and knowledgeable participants adhering more to the prescribed DOTS regimen than those with poor literacy and knowledge leading to poor adherence. The literate participants may be more aware of the consequences of non-adherence to the DOTS regimen compared to those of the illiterate and poor knowledge participants.

The results of the current study, showed a strong association between participant adherence and their place of residence, whether they lived in an urban or rural location ($p=0.001$). Accordingly, the participants in urban areas were more adherent than those in rural areas since they had easier access to DOTS centers for their medication, which is similar to the study done in Gandaki Province of Nepal [15].

Contrary to a study conducted in Uganda, which found a strong correlation between the treatment phase and non-adherence, the DOTS regimen's adherence in the present study was not significantly influenced by the phase of therapy (intensive or continuous). The likelihood of non-adherence to a regimen was approximately 6.2 ($p=0.001$) times higher for participants in a continuous phase than for those in an intensive phase in Uganda [12]. Similarly, non-adherence was high during the continuation phase of treatment in a study in Gondar, Ethiopia [16]. Another study showed that participants in the continuous phase were 1.52

times (p=0.003) more non-adherent than those in the intensive phase [22]. This difference might be because, during the intensive phase, people frequently experience severe illness and are encouraged to take their medications.

In this study, adherence was not significantly associated with the presence or absence of the symptoms. However, a study in Gandaki province of Nepal reported a statistically significant association between adherence and the presence or absence of TB symptoms [15]. Participants who were aware of the symptoms of TB were more than two and half times more likely to adhere to medicine than participants who were unaware of the symptoms of TB.

Experience of adverse drug reactions was significantly associated (p<0.001) with adherence to the regimen prescribed. Along the same line, studies done in the Eastern terai region and Gandaki province of Nepal also had a similar confounding association of adverse effects observed with adherence [15,22]. On the contrary, a study conducted in Uganda that did not show any significant association of adverse effects with non-adherence may be due to adequate counseling to expect the adverse events [12]. In our study, more the adverse effects observed, the more was the non-adherence, which could result from inadequate counseling of potential side effects of such medications.

In the present study, the incidence of ADRs was reported in 34.12% of the participants, unlike the incidences of 12.27% in Nepal [23], 17.02% in India [24] and 15% in China [25]. It might be because these studies were retrospective; hence, certain minor ADRs might not have been documented. Hence the incidence of ADR varies greatly depending on the region and time of the study.

The limitation is that the results of the current study may not apply to the broader population due to the limited sample size used. In order to link the precise statistics for adherence to the effectiveness of the DOTS regimen, we should have monitored the participants until the end of the regimen. Only two DOTS centers were used to collect the data.

CONCLUSIONS

The prevalence of adherence to the DOTS regimen was found to be high (93.5%), which is favorable for TB patients treatment outcomes. Forgetfulness, the experience of adverse drug reactions, and the transport difficulty to reach the health facility were the major reasons for poor adherence to the DOTS regimen, which can be minimized by proper patient counseling.

ADDITIONAL INFORMATION AND DECLARATIONS

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Data Availability: Data will be available upon request to corresponding authors after valid reason.

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