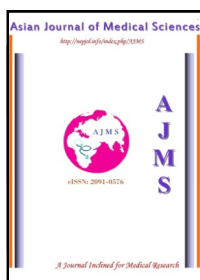# ASIAN JOURNAL OF MEDICAL SCIENCES

Adherence to Anti-Retroviral Therapy among People Living with HIV and AIDS in Far West, Nepal

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Abstract

Objective: Adherence to Anti-Retroviral Therapy is a principal predictor for the success of Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) treatment. It remains as a challenge to AIDS treatment and care with the wide spread of the associated risks. The study aims to assess adherence level and factors associated with adherence to Anti-Retroviral Therapy (ART) among people living with HIV and AIDS in Far West, Nepal.

Material & Methods: A cross sectional study was carried out in Far West between May 2009 to September 2009. A total of 176 samples allowed with 95% CI and 5% error proportionately from four ART sites were drawn. Random sampling technique was used to recruit patients. Semi-structured questionnaire schedule adapted from the Adult AIDS Clinical Trials Group (AACTG) was used and pre-tested to collect data on drug adherence. We compared non-adherent patients with adherent patients and associations with key risk factors were determined.

Results: An overall self reported adherence for a month was 84%. Those who were more than 95% adherent responded that use of watch, electronic devices such as mobiles, watch and calendar facilitated them to take the drugs regularly. Improved adherence was significantly determined by time to reach the health faility at terai (OR: 2.86, 1.10-7.47), disclosing of the HIV status (OR: 3.25; 1.02-10.19), the perceived positive benefits of ART (OR: 21.07; 6.79-68.04) and excellent satisfaction with the provider (OR: 13.11; 4.75-36.19). Travel cost more than 2$ (OR: 9.84; 3.44-28.73) was significant barrier to adherence.

Conclusion: Timely detection of non-adherence behaviours and understanding of patients' difficulties with ART could potentially help patients for adherence and therefore improve the treatment outcomes in rural hilly Nepal. Government's initiatives towards moral support for encouraging to join support group including discussions of side-effects, and everyday problems in sticking to a regimen and financial support to PHLA should be promoted to optimize the adherence rate.

Key Words: Adherence; ART; PLHA; Far West Nepal

1. Introduction

It is estimated that 4.7 million people in Asia are living with Human Immunodeficiency Virus (HIV), including 3, 50,000 who became newly infected last year.[1] Asia's epidemic peaked in the mid-1990s, and annual HIV incidence has subsequently declined by more than half. In 2008, an estimated 3, 30,000 AIDS-related deaths occurred in Asia. While the annual number of AIDS-related deaths in South and South-East Asia in 2008 was approximately 12%.[2]

In the 1990s, Introduction of Anti Retro Virals (ARVs) brought new hope to people living with HIV. More recently, the increased availability of treatment has dramatically improved survival rates and lowered the incidence of opportunistic infections in people with AIDS.[3]

National Centre for AIDS and STD Control (NCASC), Ministry of Health and Population, Government of Nepal, estimated about 70,000 to be infected with HIV in Nepal with prevalence of 0.49%.[4] NCASC had launched the free ART program since February 2004 in Teku Hospital and developed ART Guideline in 2004 which attempts to represent the current state of knowledge; it is evitable

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that as HIV and AIDS is a rapidly evolving medical field. It helps for the rationale use of the drugs. Till date there are 23 ART sites where 3,423 patients are on treatment.[6] The ARV logistic system in Nepal is managed by NCASC itself with minimal co-ordination with Logistic Management Division (LMD).

Far West Hills, with one of Asia's fastest growing AIDS epidemics, account for the 16% of total HIV infections.[4] Eligible altogether 565 Patients are on the treatment from four ART sites viz. Seti Zonal Hospital, Mahakali Zonal Hospital, Doti District Hospital and Achham District Hospital.[6] The high migration rate (at least one male member from 80-90% of the household) has contributed for the rapid spread of HIV/AIDS. About 10% of the migrants returning from Mumbai, India have been tested HIV positive.[6] To ensure the treatment is progressed, adherence of patient on ART is critical. Adherence means a more collaborative process between the patient and provider. It is the act of following a course of medication in exactly the manner it is prescribed.[7] Adherence to Anti-Retroviral Therapy (ART) is second largest predictor of progression to AIDS and death after CD4 count/reduced HIV RNA replication.[8] In ART, adherence is essential for successful treatment and sustained viral control. To achieve treatment success requires near-perfect adherence to combination ARV regimens. Adherence to an ARV treatment regimen involves taking all pills in the correctly prescribed doses, at the right time, and in the right way.[9] Studies indicate that more than 95% of the doses should be taken for optimal suppression[11].The lesser degree of adherence is more often associated with the virological failure. Poor adherence is linked with the likelihood of the drug resistance and direct treatment failure.[11]

The Second-line ART is the next regimen used in sequence immediately after first-line therapy has failed (clinically, and or immunologically and or virologically).[10] Failure to first line ART is also a growing concern in Nepal with already eight cases registered on the 2nd line ART.[6]

The risk of transmission of resistant viruses and limited future treatment options due to poor adherence makes adherence a public health concern. The aim of the study is to calculate adherence rate and to determine the factors associated to Adherence to Anti-Retroviral Therapy (ART) among People Living with HIV and AIDS in Far-West, Nepal.

2. Material and Methods

A cross sectional study was carried out using both quantitative and qualitative methods to identify magnitude of adherence; and protective and risk factors to adherence to ART among HIV infected persons. The semi structured self report questionnaire schedule from Adults AIDS Clinical Trial Group (AACTG) was modified to cultural context then translated in Nepali and pre tested.[5] Study was conducted in Far West, Nepal from May to September 2009 in all four ART sites. Patients of age above 15 years and taking ARVs for at least 3 months were enrolled in the study.[13,19] Data were collected on the basis of patient self report except CD4 count which was taken from medical record.

A total of 176 samples allowed with 95% CI and 5% error proportionately from four ART sites were drawn by using formula for estimation of sample size, $n = Z^2pqN / \alpha^2(N-1) + Z^2pq$. Random sampling technique was employed among the client visiting the ART centre with the Natural Inflow to enroll a total of 176,out of which 156 records (n=156) were analyzed. Twenty records were excluded for incompleteness.

This represents a response rate of 88.6 % of the number of patients eligible for the study. Among the 20 patients who did not participate in the study, 8 declined on confidential grounds, 6 did not give any reasons, and 6 did not done have initial CD4 counts. Semi structured questionnaire schedule and In-depth Interview were conducted to collect both qualitative and quantitative data. Incentives were not offered to patients approached for inclusion to limit any bias. Adherence was recorded as missing not more than 3 doses in which patient missing less than 3 doses were called as adherent and more than 3 doses in a month, as non adherent.[10] Last hour, Last week and Last month adherence was recorded.

Data was entered in datasheet created in Statistical Package for Social Sciences (SPSS) Version 17.0 and analysed. Statistical significance was set at p < 0.05. Bivariate (Chi-square test) analyses of variables were carried out to determine the factors for adherence. The strength of association was measured using Odds Ratios (with 95% CI). Verbal informed consent was taken from each study participants following the ethical norms and values as stated in the National Ethical Guidelines for Health Research in Nepal, 2001 and the number of patients refusing recorded.

3. Results

3.1. Baseline characteristics

A total 176 patients consented and participated in the study, of which 156 records (n=156) were analyzed. Twenty records were excluded for incompleteness. This represents 88.6% of the number of patients eligible for the study.

Table 1: General characteristics of patients by geographical region

Category	Hilly (n=49)	Terai (n=107)
	n(%)	n (%)
Sex		
Male	21 (28.4)	52 (71.6)
Female	28 (34.1)	55 (65.9)
Age (years)		
<=30	21 (55.3)	17 (44.7)
31-49	25 (16.7)	83 (83.3)
>=50	3 (30.0)	7 (70.0)
Ethnicity		
Brahmin	6 (28.6)	15 (71.4)
Chhetri	17 (30.4)	39 (69.6)
Dalit	20 (29.0)	49 (71.0)
Janajati	6 (60.0)	4 (40.0)
Religion		
Hindu	49 (32.2)	103 (67.8)
Muslim/Christian	0 (0.0)	4 (100.0)
Marital Status		
Married	22 (25.3)	65 (74.7)
Unmarried	2 (50.0)	2 (50.0)
Separate	1 (33.3)	2 (66.7)
Widowed	24 (38.7)	38 (61.3)
Educational Status		
Illiterate	23 (30.7)	52 (69.3)
Can read and write (but no formal education)	8 (23.5)	26 (76.5)
Primary +	8(42.1)	19(57.9)
Secondary +	10 (50.0)	10 (50.0)
Family Type		
Joint	15 (37.5)	25 (62.5)
Nuclear	29 (26.9)	79 (73.1)
Live alone	5 (62.5)	3 (37.5)
Family Income Source		
Agriculture	32 (34.0)	62 (66.0)
Service	73 (6.8)	12 (63.2)
Labor	6 (18.2)	27 (81.8)
Others	4 (36.4)	7 (63.6)
Time since HIV diagnosis (months)		
<=12	14 (37.8)	23 (62.2)
13-48	29 (29.9)	68 (70.1)
>=48	6 (27.3)	16 (72.7)
Time since starting ART (months)		
<=12	27 (36.0)	48 (64.0)
13-48	22 (28.6)	55 (71.4)
>=48	0 (0.0)	4 (100.0)
CD4 at start of the ART		
<=200	38 (36.9)	65 (63.1)
>200	11 (20.8)	42 (79.2)

A total of 73 males and 83 females participated in the study. The mean age was 37 years with the minimum 24 and maximum 62 with the standard deviation of 7.7. There were a high proportion of patients from urban (69%) locations compared to rural (31%) with having highest number of patients from Dalit ethnicity of 69 (44%).

3.2 Adherence to the treatment

About 17% of patients delayed more than 1 hour to take the pills and 3% have missed to take the drugs during the last week with adherence rate 97.4%. A total of 32 patients have missed to take at least single pill within the last month. Eighty four percent of the participants had more than 95% adherence and 16% respondents were less than the optimum adherence (i.e. 9% for 80-95% and 7% for < 80%), accounting for the 84% adherence rate within the last month.

3.3 Associated factors

Among the patients who have less than 95% adherence the major barrier for the adherence were busy in work and lack of knowledge of ART. Among the patients who never missed to take the pills, 52% reported that watch was useful to recall drug taking time and 27.4% family helped them to take the pills regularly.

Patients residing in the terai (ART site of Dhangadhi and Mahendranagar) area are more than thrice likely to report adherence than the client residing at the hilly area(ART site of Accham and Doti) (OR: 2.86, 1.10-7.47). Married were not different in their reported adherence compared to never married patients (OR: 5.61, 0.53-69.61).

Among the adherent group, 98.5% belong to the Chhetri community and 2% were from other religions. For the analysis, brahmins, chettri were placed in the advantaged group and other caste were placed in the disadvantaged group however, there was no difference in the reported adherence between these two groups (OR: 1.07, 0.45-2.51). Literate patients were more adherent to the regimen than the illiterate ones with 53% and 47% respectively. However, no significant association was found between the education status and adherence (OR: 1.46, 0.57-3.76).

Patients reported of prior alcohol habit were around 4.5 times less likely to adhere to the ART. Significant association was observed between the Prior alcohol habit and reported adherence rate (OR: 4.5, 1.547-12.79). Similarly the prior smoking habit was associated with the reported adherence (OR: 3.5, 1.33-9.45). No association was observed between the current alcohol habit and adherence to treatment (OR: 1.6, 0.40-5.91). Similarly, current smoking

habit and adherence to treatment was not associated with adherence to treatment (OR: 0.43, 0.95-1.962).

Table 2: Patient's medication adherence and associated factors

Variables	Adherent		Non Adherent		Odds ratio	P-value*
	n	%	n	%	(95% CI)	
Gender						
Male	63	48.1	11	44.0	1.18 (0.46-3.03)	0.71
Female	68	51.9	14	56.0	1	
Age (years)#						
> 35	76	58.0	11	44.0	1.76 (0.69-4.54)	0.20
<= 35	55	42.0	14	56.0	1	
Residence						
Terai	95	72.5	12	48.0	2.86 (1.10-7.47)	0.01
Hilly	36	27.5	13	52.0	1	
Marital Status						
Ever married	129	98.5	23	92.0	5.61 (0.53-69.61)	0.06
Unmarried	2	1.5	2	8.0	1	
Religion						
Hindu	129	98.5	23	92.0	5.61 (0.75-41.84)	0.12
Others	2	1.5	2	8.0	1	
Caste						
Advantaged	65	49.6	12	48.0	1.07 (0.45-2.51)	0.88
Disadvantaged	66	50.4	13	52.0	1	
Education status						
Literate	70	53.4	11	44.0	1.46 (0.57-3.76)	0.39
Illiterate	61	46.6	14	56.0	1	
Type of Family						
Single	100	76.3	16	64.0	1.81 (0.66-4.91)	0.20
Joint	31	23.7	9	36.0	1	
Employment Status						
Employed	25	19.0	11	44.0	0.30 (0.11-0.81)	0.07
Unemployed	106	81	14	56 .0	1	
Commuting						
By vehicle	124	94.7	22	88.0	2.42 (0.58-10.06	0.213
By foot	7	5.3	3	12.0	1	
Travel Cost/Visit(2 way)**						
<=2$	116	84.6	11	44.0	9.84 (3.44-28.73)	0.000
>2$	15	15.4	14	56.0	1	
Patient satisfaction						
Excellent	121	92.4	12	48.0	13.11 (4.75-36.19)	0.000
Good/Fair/Poor (Not Excellent)	10	7.6	13	52.0	1	

*chi-square was applied
**classified according to median values
1 $= NRs 73 (Nepal Rastra Bank, 14th March, 2010)

Around 76% of the client reporting higher adherence belongs to the single family and only 24% of the client reporting adherent belonged to joint family (Table 2). Those patients who had to pay less than 2$ per visit were around 10 times more likely to adhere to the treatment therapy than those who had to pay more than 2$ per visit (OR: 9.84, 3.44-28.73).

For around 85% of the patients service provided was excellent ('Yes' to more than 5 health facility related statements), whereas 15% responded that the service was not good. The patients who are very satisfied with the services were 13.1 times more likely to adhere to the ART. A significant association was observed between the adherence and patient satisfaction (OR: 13.1, 4.75-36.19).

Table 3: Distribution of side effects (n=89)

Side Effects	Percent
Fatigue	8.6
Vomiting	7.9
Diarrhea	4.5
Anemia	4.1
Dizziness	14.2
Headache	14.2
Arthritis	10.5
Skin rashes	9.4
Nausea	6.7
Confusion	4.1
Insomnia	0.4
Fever	7.1
Others*	8.2
Total	100

Note: Multiple response analysis was done
*Includes sleeping disorders, loss of appetite and hearing loss.

Patients who experience the side effects (72%) are found to be more non-adherent than those patients who did not experience any form of side effects (8%). The relation observed was non-significant (OR; 2.71, 0.85-5.55). Among the patients who experienced the side effects, majority (14.2%) of the patients reported dizziness and headache. Similarly, 10.5% reported arthritis and around 4.5% reported diarrhoea and 4.1% reported of anaemia (Table 3).

4. Discussion

The overall adherence rate for 1 month was found to be 84% which is similar to those reported from India[8] and other developing countries like Senegal[25], Ethiopia[18] and South Africa[26]. Achieving 100% adherence to ART among all patients is still a challenge in the Far West of Nepal. It was evident that patients took home the doses, but did not take them at the scheduled times because were busy in work and lack of knowledge of ART.

Similar to other studies elsewhere[17,20-22] age, sex, marital status, education level and employment status were not affecting adherence to treatment. However higher education status was reported to be better adherence to treatment.[22] Patients from the hilly area had poor adherence than that of client from Terai region, probably due to transport and time costs. This

suggests that patients would benefit if ART services were available in more institutions located closer to beneficiaries' homes. Study of Botswana reported that adherence difficulties related to the financial demands of therapy and an inability to afford medicines for varying periods.[19]

Access to the antiretroviral therapy was a predominant predictor of the adherence rate among the patients. Patients residing at the Terai belts with easy access to transportation and health facility were significantly associated with better adherence than that of client residing at the hilly areas with difficult terrain and longer distance from the health facility.

Interlinked with the area of residence is the travel cost associated with the visit to the health facility. A significant association was found between the travel cost and poor adherence. Financial burden was also reported to be a major reason for non adherence in India.[8] Studies conducted in Africa[26] reveal that the cost of medication is one of the most significant barriers to treatment adherence. In Botswana[19], it was also reported that adherence difficulties related to the financial demands of therapy and an inability to afford medicines for varying periods. Though Antiretroviral Therapy is provided free of cost in Nepal[10], clinic visits cost money which may stretch an already meagre budget, thus increasing the likelihood of missing the pills in lack of travel cost in resource-poor countries like Nepal.

Prior alcohol and smoking habits was associated with poor adherence similar to that of Ethiopia.[18] Alcohol and smoking habit adversely affect person's ability and skills in adhering to the treatment in both the studies. Disclosure of their HIV status is associated with the better adherence. Social or family support, peer interaction, and better physical interactions and relationships are characteristics of patients who achieve optimal adherence.[17] Social and family support, peer interaction, better physical interactions and relationship is achieved only when the client discloses his/her status. Studies[27] suggest that people cope better, if they share their HIV status. Moreover, once disclosed they usually do not fear to take drugs at the scheduled time which may have helped in improving their adherence. Support group on ARV therapy should be organized for people living with HIV and AIDS to enable discussion of disclosure, psychological issue and barrier to adherence.

Being away from home, forgetting, being too busy, stigma attached to ARVs, side effects, feeling sick were found as the most common reason for missing the pills which were almost identical to those found in other studies[14]; Several studies[15] have shown that being away from home, being too busy and forgetting is closely interrelated. Use of reminders such as the watch, mobiles and other electronic devices facilitated to take the pills regularly and timely among the client with optimal adherence. So, provision of such reminders can help in achieving optimal adherence.

5. Conclusions

The adherence 84% seems to be encouraging; however achieving adherence for all the patients on ART is a great challenge. Disclosure of the HIV status by the client, perceived benefit of the treatment, satisfaction from the service provider was found to be the facilitator for the adherence. Factors such as the prior alcohol and smoking habit, topographical difficulties and most importantly the financial cost associated with medications was identified as the barriers to the antiretroviral therapy.

Timely detection of non-adherence behaviours and appropriate monitoring of patients' difficulties with ART could potentially help patients to maintain adherence and therefore improve the treatment outcomes. Adherence is a process, not a single event, and adherence support must, therefore, be integrated into regular clinical follow up. Investigation of factors related with long-term adherence would require longer follow-up than the present study.

In order to maximize the benefit of ART, patients should be educated on the need of adhering to the right dose at the right time as an intervention against barriers to adherence. We suggest further research should investigate the cause of disparity in adherence between refill and time of taking ARV drugs, utilization of multiple measures of adherence to be incorporated in the care plans and multiple-target interventions focused to resolve the barriers to adherence should be implemented based on barriers present.

Government's initiatives towards financial and moral support to PLHA should be promoted to overcome the financial barrier and optimize the treatment adherence. Further study should be carried out to fill the gap. Future studies should be conducted for better understanding and interventions.

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