Treatment Adherence to Antiretroviral Therapy (ART) Among Human Immuno Deficiency Virus (HIV) Patients Attending the ART Centre; Kailali, Nepal : A Mixed Method Study

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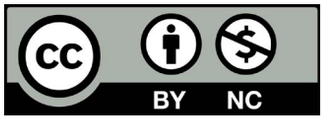

ABSTRACT

Introduction: Antiretroviral Therapy (ART) is life saver and key determinant for prognosis and quality of life for Human Immune Deficiency Virus (HIV) infected patients, reduced disease progression rate and death. Maintaining optimal adherence level aimed for long term poses significant challenge for both patients and healthcare provider.

Method: A cross-sectional facility based mixed method study was conducted, measuring 240 ART-prescribed patients and 6 in-depth interviews of service providers. Adherence was assessed through self-report from interviews. Bivariate analysis model was used to find factors associated with adherence, accompanied by thematic analysis of interview records.

Results: Adherence level was 82.8% (n=197); 83.04% in male and 81.1% in female respectively. The reasons for non-adherence were forgetting (72.8%), busy schedule (41.9%), distant ART center (11.1%), travelled out (11.1%) and acute illness (7.4%). Monthly family income, illicit drug use, treatment satisfaction and duration of drug intake were significantly associated with adherence status. Factors associated with adherence were unemployment, drug abuse, duration of drug intake, side effect, stigma and discrimination, LTFU (Loss to Follow-up) cases, poverty, and education.

Conclusion: The level of ART adherence among is unsatisfactory. Despite free access to ART medicine, it remains a major challenge to achieve complete adherence.

Keywords: Antiretroviral Therapy (ART); Adherence; Seti Zonal ART Centre; HIV positive patients; Mixed Method

INTRODUCTION

In just a few decades, HIV has become one of the most serious infectious diseases the world has faced, taking the lives of over 25 million people.[1] While this impact has been devastating, there have also been major breakthroughs in treatment. One of the most important advances is the development and growing use of antiretroviral therapy (ART), which has dramatically improved the lives of people living with HIV. ART works by controlling the virus, helping to restore the immune system, and allowing people to live longer and healthier lives.[2] But to get the full benefit of ART, it's not enough just to have access to medication, people need to take it consistently. Adherence to ART is one of the most important factors in making sure the treatment works. When taken properly, ART can reduce the risk of illness and even lower the chances of passing the virus to others. Unfortunately, sticking to the treatment isn't always easy. Even though free antiretroviral (ARV) drugs are now widely available, many people still face real challenges in following their treatment plans. [3] These challenges can include side effects from the medication, stigma from others, lack of support, mental health struggles, or simply the difficulty of getting to a clinic regularly. That's why this study set out to understand how well people are adhering to ART and what kinds of factors might be making it harder or easier for them to stay on track with their treatment.

METHODOLOGY

A cross-sectional facility based descriptive mixed method (quantitative and qualitative) approach was used to identify the level of ART adherence and factors associated with adherence to ART among HIV infected respondents who are enrolled for ART. The semi-structured questionnaire was developed from the literature and modified after pilot study and translated in Nepali. Interview guideline was also developed from literature and used for qualitative data among ART service providers which include Doctor, 2 ART counselor, ART coordinator and ART focal person. Study was conducted in Seti Zonal ART Centre from January to March 2017. Data were collected on the basis of respondent's self-report and for qualitative part, service providers perspective on ART adherence was assessed through in-depth interviews. The total 240 samples were collected by using cochranc's formula considering the prevalence of adherence 84% from a study done in Far western region of Nepal, with 95% CI, design effect (δ) 2 and non-response rate of 10%.4 Purposive sampling method was employed among the HIV infected patients who visit ART center to refill their ART medication. The dependent variable was adherence to ART and independent variables were socio-demographic (age, sex, income, gender, marital status etc.) and medical characteristics (duration of ART drug intake, treatment regimen and pill/day). Adherence was based on self-report of missing doses in 15 days prior to study; missing doses from 1 dose to more than 4 doses were identified. >95% compliance is assumed as perfect adherence, <2 doses missed as adequate adherence and more than 3 doses missed as non-adherence. Data was entered in Microsoft Office package version 10 and was analyzed by using SPSS version 16.0 and analyzed. Statistical significance was set at $p < 0.05$. Bivariate (Chi-square test and Likelihood ratio) analyses of variables were carried out to determine the factors for adherence. The strength of association was measured using Odds Ratios (with 95% CI). For qualitative data audio recordings of in-depth interviews was translated and transcribed from Nepali language into English. Thematic content analysis was carried out; data was coded, categorized and common themes were identified as per research questions. Ethical clearance certificate was taken from Institutional Ethical Committee K.S Hegde Medical Academy, Nitte University. Approval letter from Hospital authorities was taken prior to conducting study. Verbal and written informed consent were taken for each study participants following ethical norms.

RESULTS

QUANTITATIVE RESULTS

Socio-demographic and socio-economic characteristics

A total 240 ART users were interviewed and 100% responded; 52.9% were female, majorly were in age group 40–59-year, mean age of 41 year and standard deviation 11.56 year. 56.67% were married, 97.08% were Hindu, 50% were illiterate, 42.03% were unemployed, 69.6% have nuclear family, 54.6% falls in NRs 5000 -12000 monthly family income category, 80.8% travel ART center via Bus and the 73.3% respondents spent less than NRs150 to reach ART center. (Table 1 and 2)

Medical history of patient

70.42% said that counseling form health worker was the deciding factor for HIV test. Around one third 75% (n=180) were in ARV therapy form more than 3 years and 0.2% (n=2) were enrolled from less than a month. Near one third 70% (n=168) respondents felt improvement in their health after starting treatment and 2.1% and 0.4% fells same and worse respectively. Treatment regimen was changed in 20% (n=48) respondents; major reasons for changing treatment regimen were side effects 52.9%, treatment efficiency 37.3% and other reasons 7.8%. (Table 3)

Table 1: Distribution of Socio-Demographic Characteristics (n=240)

Variables	Categories	Frequency	%
Age	**<19**	**13**	**5.4**
	20-39	73	30.4
	40-59	142	59.2
	>60	12	5
Sex	Male	112	46.7
	Female	127	52.9
	Third gender	1	0.42
Marital Status	Married	136	56.67
	Unmarried	18	7.5
	Divorce	1	0.42
	Widow/Widower	85	35.42
Religion	Hindu	233	97.08
	Buddhist	1	0.42
	Muslim	2	0.83
	Others(specify)	4	1.7
Education	Illiterate	120	50
	Primary education	85	35.42
	Secondary education	28	11.7
	Higher Secondary education	7	2.92
Family size	Nuclear	167	69.6
	Joint	71	29.6
	Live alone	2	0.8
Transportation to ART center	By bus	194	80.8
	By walk	12	5
	Two-wheeler	22	9.2
	Others (specify)	12	5

Table 2: Distribution of Socioeconomic Characteristics (n=240)

Variables	Categories	Frequency (n)	Percentage (%)
Occupation	**Unemployment**	**101**	**42.03**
	Agriculture	63	26.25
	Labor worker	15	6.25
	Business	15	6.25
	Office worker	15	6.25
	Student	13	5.42
	Others(specify)	18	7.5
Monthly family income (NRs)	Below 5000	85	35.42
	5000-12000	131	54.6
	12000-20000	19	7.2
	20000 and above	5	2.1
Travelling Cost (NRs)	0-150	176	73.3
	151-300	53	22.08
	301-450	7	2.92
	451-600	3	1.25
	>600	1	0.42

Knowledge about the treatment

Respondents were inquired about ART treatment, treatment adherence, its importance and the effects of ART non-adherence to find out the knowledge on ART. Of the total, 65.8% know the role of ART. Regarding knowledge on treatment combination less 18.75% (n=45) respondents have adequate knowledge. All of them are well knowledgeable about the prescribed medicines. All said treatment adherence is important and the reasons illustrated as 93.30% reduce viral load, 25.4% for normal lifestyle and so on. All had heard about effect of non-adherence at some point from doctors, counselors and also from Community & home-based care workers (CHBCW). Around four fifth (n=189) said drug resistant was one effect of treatment nonadherence, 55.8% said, deterioration of health followed by 20.42 % early death and 1.2% other reasons (Table 4). The knowledge about ART based on above variables; total variables were 13 and the median value is 9; less than median is considered as poor knowledge and more than median value is good knowledge. (Figure 1)

Adherence of ART

Adherence is calculated by number of doses missed in period of 15 days prior to study. Adequate adherence is calculated from number of 1-2 doses missed and non-adherence was measured from missed more than two doses. Among all, 66.66% (n=160) reported perfect adherence (≥95%), adequate adherence 15.42% (n=37) and 17.92% (n=43) were non adherent. The adherence prevalence among men and women was 83.04% and 81.1% respectively. (Figure 2) Respondents those reported missing doses last week (n=80) were further asked to assess the reasons for treatment non-adherence. The most frequently cited result was "forgot" and "busy in work" (Table 5).

Table 3: Medical history of patient (n=240)

Variables	Categories	Freq (n)	(%)
Reasons to decide for HIV testing*	**Illness**	**48**	**20**
	Weight loss	17	7.08
	Health Camp	36	15
	Counseling from health workers	169	70.42
	Others specify	16	6.7
Duration of Enrolling in ART	Less than 1 month	2	0.8
	1-6 months	8	3.3
	6 month- 1 year	15	6.3
	1-3 years	35	14.6
	3 years and above	180	75
Health status after treatment started	Improved	168	70
	Normal	66	27.5
	Same	5	2.1
	Worse	1	0.42
Change in treatment regimen after starting ART	No	192	80
	Yes	48	20
Reasons for changed Treatment regimen (n=48)	Treatment inefficiency	19	37.3
	Side effects	27	52.9
	Didn't want to cont. treatment	1	2.0

** Multiple answers*

Table 4: Knowledge about the Anti-Retroviral Treatment (ART (n=240)			
Variables	**Categories**	**Freq (n)**	**(%)**
Know about ART	**Yes**	**240**	**100**
Familiar about the role of ART	No	82	34.2
	Yes	158	65.8
Knowledge on combination ART treatment	No	23	9.6
	Yes	45	18.75
	Don't know	172	71.7
Know about ART medicine prescribed to respondents	Yes	240	100
Familiar about ART adherence important to treat HIV/ AIDS	Yes	240	100
Importance of ART adherence *	To reduce the viral load	224	93.3
	To reduce therapeutic failure	61	25.4
	To reduce risk of HIV transmission	1	0.4
	For normal lifestyle	101	42.1
Know about the effect of treatment non-adherence*	Yes	240	100
Effects of treatment adherence	Drug resistant	189	78.8
	Deterioration of health	134	55.8
	Early death	49	20.42
	Others (specify)	3	1.2

** Multiple answers*

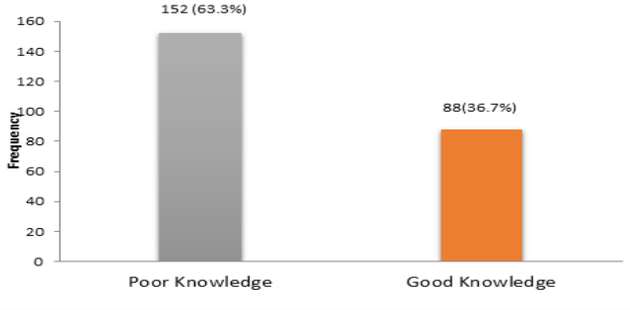

Figure 1 Knowledge about Anti-Retroviral Treatment

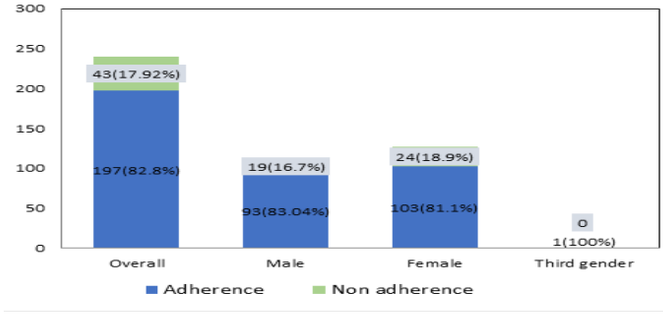

Figure 2 : Proportions of HIV/AIDS patients with ART therapy adherent status

Associated factors for Adherence

Among all the associated factors for medication adherence monthly family income (p=0.0042), illegal drugs use (p=0.012), treatment satisfaction (p=0.001) and duration of drug intake (<0.001) were significant difference with the adherent status with the level of 0.005% significance. (Table 6 and 7)

Table 5: Knowledge about the Anti-Retroviral Treatment (ART) (n=240)

Variable	Frequency (n*)	Percent (%)
Reasons for missed medicament		
Busy in work	34	41.98
Forgot	59	72.84
Didn't got fed the medicine	9	11.11
Distant ART center	9	11.11
Travelled out	8	9.88
Acute Illness	6	7.41
Others (specify)	1	1.23

Table 6: Socio-demographic factors associated with treatment adherence

Variables	Categories	Total	Adherence	Non Adherence	P-value
n (%)	**Non-adherence n (%)**				
Age	<19	13	10 (76.92)	3(23.1)	
	20-39	73	60(82.2	13(17.8)	
	40-59	142	118(83.1)	24(16.9)	0.894
	>60	12	9 (75)	3(25)	
Sex	Male	112	93(83.04)	19(16.96)	
	Female	127	103(81.1)	24(18.9)	0.785
	Third Gender	1	1(100)	0 (0)	
Marital Status	Married	136	112(82.35)	24(17.65)	
	Unmarried	18	12(66.67)	6 (33.3)	
	Divorce	1	1(100)	0(0%)	0.383
	Widow/Widower	85	72(84.71)	13(15.3)	
Religion	Hindu	233	193(82.83)	40(17.7)	
	Buddhist	1	0(0)	1(100)	
	Muslim	2	2(100)	0(100)	0.072
	Others	4	2(50)	2(50)	
Educational Status	Illiterate	120	99(82.5)	21(17.5)	
	Primary Education	85	68(80)	17(20)	
	Secondary Education	28	26(92.9)	2(7.1)	0.169
	Higher Education	7	4(57.1)	3(42.9)	
Occupation	Unemployment	101	85(84.16)	16(15.84)	
	Agriculture	63	54(85.71)	9(14.29)	
	Labor worker	15	12(80)	3(20)	
	Business	15	14(93.3)	1(6.67)	0.387
	Office worker	15	11(73.3)	4(26.67)	
	Student	13	9(69.2)	4(30.8)	
	Other specify	18	12(66.7)	6(33.3)	
Family Size	Nuclear	167	135(80.8)	32(19.2)	
	Joint	71	60(84.5)	11(15.5)	0.634
	Live alone	2	2(100)	0(0)	

Table 7: Socio-economic and medical characteristic associated with treatment adherence

Variables	Categories	Total	Adherence n(%)	Non Adherence n(%)	P-value
Monthly Family	Below 5000	85	64(75.3)	21(24.7)	**0.042***
Income (NRs)	Above 5000	155	133(85.8)	22(14.2)	
Means of Transportation	By bus	194	160(82.5)	34(17.5)	0.696
	By walk	12	9(75)	3(25)	
	Two-wheeler	22	17(77.3)	5(22.7)	
	Others (specify)	12	11(91.7)	1(8.3)	
Travelling Cost (NRs)	0-150	176	145(82.4)	31(17.6)	0.54
	151-300	53	44(83.02)	9(16.98)	
	301-450	7	6(85.7)	1(14.3)	
	301-450	3	2(66.66)	1(33.33)	
	600>	1	0(0)	1(100	
Time to reach ART center	0-2 Hours	179	147(82.12)	32(17.88)	0.322
	2.1-4 Hours	53	45(84.91)	8(15.09)	
	4.1-6 Hours	5	4(75)	1(25)	
	6.1-8 Hours	3	1(33.33)	2(66.66)	
Alcohol in past one month	Yes	25	19(76)	6(24)	0.402
	No	215	178(82.7)	37(17.3)	
Illegal drugs use	Yes	4	1(25)	3(75)	**0.012***
	No	236	196(83.1)	40(16.9)	
Treatment satisfaction	Yes	226	190(84.1)	36(15.9)	**0.001***
	No	14	7(50)	7(50)	
Tablets Daily	<2 Medicine/day	157	127(80.9)	30(19.1)	0.597
	>2 Medicine/day	83	70(84.3)	13(15.7)	
Duration of drug intake (yrs.)	<3yrs	59	58 (98.3)	1(1.7)	**<0.001***
	>3yrs	181	139(76.8)	42(23.2)	

** Indicates significant at the 5% level of significance.*

QUALITATIVE RESULTS

The qualitative information extracted from in-depth interviews which complemented and supported the quantitative findings. It also helps in finding out the perception regarding ART adherence from ART service providers' perspective. All had taken ART related CMT training which is helpful in handling patient clinically, and some had taken more than one training as job requirement.

"I had taken CMT (Clinical Management Training), HIV Test and Counseling (HTC) Training and Logistics Management Training after joining for the job." -IDIR5

Unavailability of drugs in ART center is a major reason for non-adherence and it's a major contributing factor also.

We will get medicines directly from NCASC (National center for AIDS and control) and other drugs (OIs) from several sources as Zonal medical store, DHO and also from Seti Zonal Hospital". -IDIR3

Predicting factors are most discussed issues in ART adherence as respondents said patient's related factors as literacy, unemployment, duration of drug intake, side effect, stigma, discrimination and drug abuse are considered predicting factor for non-adherence. Other relating factors are treatment regimen, patient-provider relationship and disease characteristics.

"For non-adherence to treatment, the reasons are unemployment, migrant workers (works in India), acute

illness, poor economy, illiteracy, social stigma, distant ART center, drug doses and duration of treatment." –IDIR1

"The major factor for maintaining treatment adherence is monitoring of cases, increasing LTF (Loss to Follow-up) cases, poverty, and education. LTFU case is mainly because of migrant workers (majority of them migrated to India in search of job), social stigma and discrimination." -IDIR5

Due to stigma and discrimination, late identification of patient, migration of case to abroad, and loss to follow of patients are the challenges faced while supporting patients to adhere for ART Treatment.

"The major challenges for maintaining treatment adherence are controlling of migrant worker, provision of education, reducing stigma/discrimination in society, lacking in social awareness, distant ART center etc. For migrant workers the need of coordination and collaboration between two countries is needed on provision of ART medicine and treatment adherence. Health education and awareness campaign regarding the avoidance of stigma and discrimination towards the HIV patients in Society"-IDIR1

"The major challenges for maintaining treatment adherence are difficult to follow up and side effects of medicine. Initial side-effects and prolonged side-effects as rashes, loss of appetite, dizziness, anemic condition etc. majorly influence in drug adherence".

"Because of stigma and discrimination, late identification of new cases, community home based care will not be effective, avoidance of treatment and it's a challenging factor for us". - IDIR3

Community home based care is effective in initial phase of ART treatment where patient face more side effects. Social support programs are also effectivein identifying loss to follow-up cases and counseling such cases to bring into ART treatment once again.

"We are coordinating with organizations like Navakiran plus, AIDS for Health, Red Cross Society; which provide home based care, screening camp to identify new cases and helping us in identifying LFU cases in community and also provide counseling to such cases". -IDIR3

Counseling to patients and enrolling and retaining them in ARV therapy, late identification and detection of patients and migration of cases to abroad be the major challenges faced during regular work.

"Major challenge encountered is to retain all the patients in this treatment and because of poverty most of male ART patients went to abroad for seeking job opportunities and providing medicines to them is a major challenge." -IDIR4

DISCUSSION

Overall self-reported level of adherence for fifteen days was 82.8%. The results shows that factors such as monthly family income, duration of drug intake (yrs.), illegal drugs use and treatment satisfaction are independently associated with adherence. The reasons for non-adherence were busy in work, forgot distant ART center and financial difficulties which correlate with other studies done in Nepal. [4-6] In this study adherence level is slightly lower, and consistent to other similar studies conducted in Nepal. [4,6-9] In this study, ART regimen and numbers of pills per day were not significant in the univariate analysis whereas in other studies they had shown these were associated with adherence, as the increase in numbers of pills and number of daily doses; adherence was decreased. [10] Similar to this study several studies conducted in Nepal reported education level didn't significantly influence non-adherence. The reasons were counseling provided from health worker about effect of non-adherence and proper follow-up. [4,6,7] Whereas, some studies conducting in Nepal shows educational status has significant impact on ART adherence. [6,7] Though, Nepal government is providing free ART medicines, respondents were getting free health related services and travel cost (after reaching ART center) in government hospitals. Yet the income is a one major determinant for ART adherence. Money emerged as a greatest barrier for most respondents in costs of transportation, health checkup. Income factor was found significant as with the study findings of Sharada P. Wasti et al. [6]

This study shows that respondents who were in treatment from more than three years more non-adherent to ARV therapy than that of respondents who were in treatment from less than three years. A study conducted in Kathmandu shows contrasting result as there isn't any significance on ART adherence between those who had treatment started from less than 24 months and more than 24 months [3]. But in another study conducted by Kathmandu shows significant association with the ART initiation time period with adherence. [6] In this study Knowledge on ART is found little less 36.7%, the reason might be most of the respondents were illiterate (50%) and also 35.42% were having primary education. The somehow similar result was obtained in the study conducted in Ghana; more than 90% of the HIV infected

women had inadequate knowledge about ART. [11] Illegal drugs use is found significant factor for adherence in various studies and it remained as the strongest predictor for non-adherence. Substance abuse is a major barrier for not taking ART medication in time because it made them relapse or forgot the timing of their medication. [6] Another study shows patients with the history of substance use were relatively less engaged to their health care provider and such respondents are likely to exhibit higher rate of refusal to treatment. [3] Treatment satisfaction is a subjective which majorly depends upon the patient-provider relationship, counseling services, trust and therapeutic relationship. In this study 5.83% respondents were unsatisfied ant they show more non-adherence too. LTFU was found major factor for adherence in this study and the similar result was found on study conducted by Bam et al. in far-western region of Nepal. Due to unemployment, low socio-economic status and low literacy rate migrant workers migrated to India in search of job; in result LTFU cases will increase in this area. [4] Social stigma and discrimination are found to be a major predicting factor for non-adherenceto ART. The similar mixed method study conducted in Nepal stated that mostly women were more influenced of it. Rejection from family/community, which generated a fear of exposure, which itself affect adherence.[6]

CONCLUSION

The level of ART adherence among the HIV patients were unsatisfactory; the reasons behind non-adherence were busy schedule, forgetting medicine, distant ART center, travelled out, acute illness, and didn't get fed the medicine. Adherence found in this study is similar as compared with qualitative findings. The quantitative findings suggested that income, ART initiation duration, use of illegal drugs and treatment satisfaction were the factors for adherence. Other factors such as education, poverty, social stigma and discrimination, treatment regimen, side effects were factors of adherence from qualitative analysis. Furthermore, the result shows that despite free access to ART medicine, it remains a major challenge for to achieve perfect adherence. Adherence to ART varies over the time and also for individuals. So, multiple measures, further longitudinal research including both user and service providers' perspective should be analyzed to conclude the factors associated with adherence.

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