

Factors associated with adherence to antiretroviral therapy in HIV-infected patients

A cross-sectional study in Kathmandu District, Nepal



Rajesh Shigdel

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Supervisor: Luai A. Ahmed

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By: **RAJESH SHIGDEL**

Supervisor: **LUAI A. AHMED** *MBBS, PhD.*

Department of Community Medicine

Faculty of Health Sciences

University of Tromsø

September 2012

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ABSTRACT

Objective: To determine the prevalence and predictors of antiretroviral therapy adherence among HIV/ AIDS patients in Kathmandu district.

Methods: A cross-sectional study of 316 HIV-positive individuals receiving antiretroviral therapy from three ART sites in Kathmandu districts was done from January 2012 to February 2012. The participants were interviewed and answered questions about socio-demographic status and antiretroviral therapy during the past week. Participants were considered adherent if they reported taking $\geq 95\%$ of their medication as prescribed. The association between explanatory variables and adherence was measured using logistic regression and was reported as odds ratio (OR) with 95% confidence interval.

Results: Out of the 316 participants, 64.6% (n=201) were men and 35.4% (n=112) were women. The adherence prevalence of the study participants was 86.7% (n=274). The adherence prevalence in men and women were 84.3 % and 91%, respectively. Age (OR 1.04; 95% CI 1.00-1.09), time taken to reach ART center (OR 1.38; 95% CI 1.12-1.71), past illegal drugs use (OR 3.98; 95% CI 1.71-9.24), side effects (OR 4.88; 95% CI 1.09-21.8), were all independently and negatively associated with adherence. Whereas, use of reminder tools (OR 3.45; 95% CI 1.33-8.91) was independently and positively associated with adherence.

Conclusion: The prevalence of adherence found in this study is encouraging. Age, time taken to reach ART center, side effects, illegal drugs use and not using reminder tools present barriers for adherence to ART. Improving adherence requires interventions which recognize these barriers.

Key Words: Antiretroviral Therapy (ART), Adherence, Kathmandu, AIDS patients

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LIST OF ABBREVIATION

AIDS- Acquired Immune Deficiency Syndrome

ART- Antiretroviral Therapy

CASI- Computer-Assisted Self-Interviewing

CCCs- Community Care Centers

CD4 - Cluster of Differentiation 4

CHBC- Community and Home-Based Care (CHBC)

DOT- Direct Observation System

D4T- Stavudine

ddI- Didanosine

EFV- Efavirenz

FSW- Female Sex Worker

GDP- Gross domestic product

HDI- Human Development Index

HIV- Human Immune Deficiency Virus

IDU- Injection Drug Users

MARPs- Most-at-risk Population

MDG- Millennium Development Goal

MEMS- Medical Event Monitoring System

MSM- Men who Have Sex with Men

MTCT- Mother to Child Transmission

NCASC- National Centre for AIDS and STD Control

NHRC- Nepal Health Research Council

NNRTI- Non-nucleoside Reverse Transcriptase Inhibitors

NsRTI- Nucleoside Reverse Transcriptase Inhibitor

NVP- Nevirapine

PC- Pill Count

PIT- Pill Identification Test

PLWH - People Living with HIV

PMTCT- Prevention of Mother-to-Child Transmission

PPP- Purchasing power parity

SPSS- Statistical Package for Social Science.

TB- Tuberculosis

3TC- Lamivudine

TDF- Tenofovir Disoproxil Fumarate

TDM- Therapeutic Drug Monitoring

VAS- Visual Analogue Scale

VCT- Voluntary Counseling and Testing

VDCs- Village Development Committees

WHO- World Health Organization

ZDV- Zidovudine (also known as AZT)

1. INTRODUCTION

1.1. Global Epidemiology of HIV/AIDS

The first case of the Acquired Immune Deficiency Syndrome (AIDS) was reported in 1981 in the USA. Within a short period of time the spread of the Human Immunodeficiency Virus (HIV) and AIDS has reached a pandemic form [1]. Now HIV has become one of the world's leading infectious killers, claiming more than 25 million lives over the past three decades [2]. Based on recent UNAIDS World AIDS day report, there are 34 million people living with AIDS across the globe, 2.67 million people became infected with the virus and 1.8 million people died of HIV-related causes at the end of 2010. The same report shows increased access to HIV treatment in last few years, and decreased new HIV infections and AIDS-related deaths to the lowest levels since the peak of the epidemic. New HIV infections were reduced by 21% since 1997, and deaths from AIDS-related illnesses decreased by 21% since 2005 [3]. These reports support the fact that the global response to AIDS has demonstrated tangible progress toward the achievement of Millennium development goals 6 (MDG 6) [4]. However, AIDS had become one of the leading causes of death among adults in sub-Saharan Africa. This region with only 12% of the global population remains as the most heavily affected by HIV&AIDS in 2010. An estimated 68% of all people living with HIV resided in sub-Saharan Africa [5]. The prevalence of HIV is comparatively lower in Asia than the other continents, but the actual size of the Asian population makes it the second largest grouping of people living with HIV [5].

The first HIV case in the Asia-Pacific region was reported from Thailand in 1984. Within a few years, HIV continues to spread in this region [6]. In late 2010, estimated 270 000 (230 000–340 000) new HIV infections are there in South and Southeast Asia. This was 40% less than at the epidemic's peak in 1996 [1]. According to data published by World Bank, between

2 and 3.5 million people in South Asia were living with HIV and AIDS in 2010. India alone accounts for 2.5 million people living with HIV and AIDS [7].

1.2 Global Response to HIV/AIDS

Introduced in 1986, Zidovudine (ZDV) was the first antiretroviral drug for treatment of HIV infected patients. Few years later, other nucleoside reverse transcriptase inhibitor (NsRTIs) drugs such as Didanosine (ddI), Lamivudine (3TC), and Stavudine (d4T) were introduced. These days, new classes of drugs; the protease inhibitors (PI) and non-nucleoside reverse transcriptase inhibitors (NNRTI), are available in order to prevent the emergence of resistance and to strength the immune function. Now, standard antiretroviral therapy (ART) consists of the combination of at least three antiretroviral (ARV) drugs [8, 9]. The ART has provided a relief to HIV-infected individuals by reducing the likelihood of opportunistic infection rather than curing the disease. Moreover, it has played an important role in decreasing the mortality and morbidity of related to HIV/AIDS [5, 10].

In 2003, the World Health Organization (WHO) had launched the ambitious target to access ART for 3 million people living in low- and middle-income countries by 2005. Though, the target was not achieved until 2007, but it was useful for expanding the ART coverage. Again In 2011, the international community committed achieving universal access by 2015 and it is also a part of millennium development goal [11]. During the last few years, global effort had been made to scale up the antiretroviral therapy in the developing countries. By the end of 2010, approximately 6,650,000 people were reviving antiretroviral therapy in low and middle income countries [12]. Sub-Saharan Africa had the greatest increase in the absolute number of people receiving ART. The estimated coverage of ART in low and middle-income countries was 47% at the end of 2010, compared to 39% at the end of 2009 [5]. It is estimated that around 2.5 million deaths have been averted in low and middle-income countries since

1995 after introducing the antiretroviral therapy. In addition to decreasing HIV- related mortality and morbidity, scientific evidence shows that increased access to ART is also reducing the risk of HIV transmission to sexual partners by 96% [13,14].

1.3 Epidemiology and response to HIV/AIDS in Nepal

1.3.1 Country profile

Nepal is a small landlocked country with multicultural, geographical richness and diversity. It lies in the central Himalayas wedged between India to its east, south and west and China to its north. It covers an area of 147,181 km². It is a homeland of 30 million people, and agriculture is the major source of economy [15]. Administratively, the country is divided into 75 districts, 58 municipalities, and 3,915 Village Development Committees (VDCs). There are over 100 ethnic groups and 92 spoken languages [16]. The country has seen many political changes in its modernization process, which have resulted in major social and economic transformations. Besides that, factor such as poverty; political instability, deprivation, and discrimination are core underlying causes of poor development. Despite the above hindering factor and decade-long conflict Nepal is close to achieving several of the eight MDGs by 2015 [17]. Demographic profile of the country is presented in Table 1.

1.3.2. Epidemiology of HIV/AIDS in Nepal

According to the World Bank, “HIV in Nepal is extremely heterogeneous, with respect to the most-at-risk populations (MARPs), geographic distribution, and risk factors in different geographic regions” [7]. Since the first case of AIDS was reported in 1988, HIV in the country has evolved from “low to concentrated epidemic” [19]. Recent report shows that approximately 50,200 adults and children are living with HIV. The overall prevalence of HIV among adult, aged 15-49 years was estimated to be 0.30% [20]. Of this, an estimated 28.5%

were women and 58% were men belonging to reproductive age group. “However, World Bank report suggests that due to limitations of Nepal’s public health surveillance system, the actual number of infections is could be even higher” [7].

Table 1: Demographics profile of Nepal [15,18].

Total Population both sexes (In thousands)	30,485.5
Annual Population growth rate	1.596% (2011 est.)
Population aged (Thousand)	15-64 years 61.1% (male 8,607,338/female 9,344,537)
Percentage of population in urban areas	19% (2010)
Crude birth rate (births per 1000 population)	25.4 (2008)
Under-5 mortality rate (per 1000 live birth)	51 (2008)
Human development index (HDI)	0.458 (2011) Rank 157
Life expectancy at birth (Years)	67.5 (2010)
Adult literacy rate	57.9 (2008)
Ratio of girls to boys in primary and secondary education (%)	82 (2002)
GDP per capita (PPP,\$US)	\$1,300 (2011 est.)
Total health expenditure	5.5 % of GDP (2010) i.e 66 (per capita,ppp US\$)
Prevalence of HIV among young population	0.30% (2012)

The major mode of transmission of HIV is through heterosexual behavior, where four out of every five infections, are transmitted sexually [7]. The estimated HIV prevalence amongst MARPS are: Male labour migrants (27.6 %),Men who have sex with men (MSM) (14.4 %), Male sex workers, transgender and their clients (MTCs) (7.2 %), female sex worker (FSW) (1.5%). client of female sex workers (4.4 %), injection drug users (IDU) (2.2%) and the remaining male and female populations who are identified as low risk population accounted for 16% and 27%, respectively [21,22]. Generally, FSW, IDU and MSM are considered as key population who are at a higher risk of acquiring HIV infection. While the clients of sex worker and male labour migrants are playing the role of bridging populations for transmission of HIV between high risk group and the general population [23].

New HIV infections have significantly reduced since last 5 years due to targeted prevention intervention among MARPS. However, it is still a challenge to improve the effective coverage of prevention intervention and to achieving the national target of reducing the new HIV infections into half by 2015[23].

1.3.3 Nepal's Response to HIV/AIDS

The Government of Nepal started HIV/AIDS treatment program since 2004 and started giving free ART drugs from Teku Hospital only for limited number of patients.[24] Now, the government is providing free of cost ART service and counseling for all those in need, through different ART centers and ART Sub-center (in public hospitals and other non-governmental organizations). There is a national ART guidelines and standard operating procedure for the clinical management of ART in Nepal [10,24] Nepal's first ART center, Teku is operating with different service outlets such as counseling, voluntary counseling and testing (VCT), pre-ART and ART. During the last few years, the number of patients on ART has consistently increased following WHO recommended ART eligibility to patients with CD4 below 350 cells/mm³ [15]. The total ART coverage reached 23.7 % by December 2011, and 6,051 adults, and 432 children were accessing ART from 26 ART centers and 10 sub-ART centers throughout the country. Similarly, CD4 count service is available at 13 centers while 4 centers have CD4 caliber. Among subjects with advanced HIV infection who are currently receiving ART, 57.8% are males, 42% are females and 0.92% are of third genders [24]. In the past few years, the HIV prevention program has focused the high risk group population and consequently Nepal has been successful in reducing the incidence of HIV infection through both providing treatment and preventing vertical (mother-to-child) transmission (MTCT) of HIV. Furthermore, the Government of Nepal has shown its commitment for the virtual elimination of MTCT of HIV by 2015. Different activities and

programs have been implemented through ART centers to improve the adherence to ART and follow-up of people living with HIV/AIDS (PLHIV). Some of the examples are establishment of community and home-based care (CHBC) site, Community Care Centers (CCCs) to provide care, support and treatment to PLWA in some districts. However, it is still challenging to a resources-limited country like Nepal, to achieve 80% of universal access to those who require ART in the next few years [23].

There are several regimens available with acceptable antiretroviral potency, generally, the following regimens: Zidovudine/Lamivudine/Efavirenz, Zidovudine/Lamivudine/Nevirapine, Stavudine/Lamivudine/Nevirapine, Stavudine/Lamivudine/efavirenz, are commonly used as first line drugs and Tenofovir/Lamivudine/Efavirenz, Tenofovir/Lamivudine/Efavirenz used as second line drugs in Nepal. Furthermore, the choice of regimen depends on availability, convenience and likelihood of adherence, regimen potency, tolerance etc. [8].

1.4. Adherence to ART

In the context of treatment with medications, adherence is defined as a patient's ability to follow a treatment plan, take medications at prescribed times and frequencies, and follow restrictions regarding food and other medications [25]. Adherence is a primary determinant of the effectiveness of treatment [26]. It is also considered as a major predictor of the survival of individuals living with HIV/AIDS [27]. More than 95% adherence is required in ART in order to prevent the emergence of resistant viral strains. In practice this degree of adherence requires a patient on a twice-daily regimen to not miss or substantially delay more than 3 doses of antiretroviral medications per month [8]. Adherence to antiretroviral therapy (ART) has been strongly correlated with HIV durable viral suppression, reduced destruction of CD4 cells, reduced rates of resistance, increased in survival, and improved quality of life [27,28].

The availability of antiretroviral treatment (ART) has dramatically improved the prognosis and quality of life for HIV/AIDS patients, and reduced the rate of disease progression and death. However, increased access to ART has been accompanied by increasing unsatisfactory adherence levels and the potential risk of drug resistance. Maintaining an optimal adherence level for a long term poses a significant challenge for both patients and health care provider [29]. Suboptimal treatment can lead to drug failure with the latter resulting in spread of drug resistant mutation. Consequently, it can create dangerous public health situation and decrease the success of available HIV treatment [30]. Moreover, if people living with HIV require second-line treatment, it can be ten times more expensive than first line drugs. It also leads to increased hospitalization rate, increased the cost of health care, effects on human resources productivity, disruption of family and communities and morbidity and mortality in developing countries [31].

There are various factors affecting adherence, which generally are related to characteristics of the patient, the regimen, the clinical setting, the society and the relationship between the service provider and the patient [8, 27]. Presently, poor adherence to treatment regimen remains a major obstacle in the fight against HIV/AIDS [28]. Without proper treatment and prophylaxis, HIV/AIDS presents a significant challenge to global tuberculosis (TB) control. Whereas, TB is a leading preventable cause of death among people living with HIV and it is estimated that without proper treatment, the lifetime risk of developing active tuberculosis among the people with HIV is 30 times as compared to the people without HIV [1].

1.4.1. Predictors of Adherence

a) Patient Characteristics

Patient's related factors are the most important factors that influence their adherence and are under the patient's control. Understanding them is important in order to improve the

adherence [32]. In addition, the cultural aspects of the patient's health beliefs and life goals are also important influential factors in the context of treatment adherence [33].

Studies have shown controversial associations between socio-demographic factors and adherence behavior.[28,29,30] Though some studies have found that male gender, older age, higher income, higher education, and literacy correlate with better adherence [34]. More consistent associations are found between certain psychosocial factors and adherence behavior. Common predictors of non-adherence include depression/psychiatric morbidity, active drug or alcohol use, side effect, stigma and discrimination, stressful life events, lack of access and social support etc [35].

b) Treatment regimen

Characteristics of the medical regimen constitute another important correlate of adherence. Factors related to the treatment regimen include the number of pills prescribed, the complexity of the regimen (dose frequency and food instructions), the specific type of antiretroviral drugs, and the short and long-term medication side effects [35]. Adverse medication side effects, complexity of daily routines, pill burdens, lowered genetic barriers leading to drug-class resistance, and long-term uncertainties are all major factors that challenge a patient's ability to successfully adhere to a regimen [36].

c) Patient-provider relationship:

Patient-provider relationship can also affect adherence. Trust in the provider and clinical staff, good communication, adequate education about medication, the provider's willingness to include the patient in the decision-making process, the affective tone of relationship may affect the adherence, including the patient's overall satisfaction [35]. Overall patient satisfaction with medical care has been found to correlate with increased adherence. The perception of providers as being warm and caring has been related to greater adherence [33].

d) Disease characteristics

Disease characteristics include the stage and duration of HIV infection, associated opportunistic infections, and HIV-related symptoms [35]. Some studies described an increased adherence in those with the history of opportunistic infections. This shows that prior opportunistic infections increased adherence suggesting that illness severity motivated patient's adherence [36, 37].

1.4.2. Measurement of adherence

There is no gold standard to assess adherence, therefore, it is difficult to accurately measure adherence to therapy [27]. However, there are many validated tools and strategies to assess adherence. Currently, available methods for adherence assessment can be grouped into two major categories (Table 2) [38].

Table 2: Different measures of adherence

Direct Measures	Indirect measures
Direct observed Treatment (DOT)	Pharmacy records
Therapeutic drug monitoring (TDM)	Self-report (Including Computer-Assisted Self-Interviewing [CASI])
Biomarkers	Pill count (PC)
Medication Event Monitoring System (MEMS)	Visual analogue scale (VAS)
	Pill identification test (PIT)

a) Direct observation therapy (DOT)

The DOT method requires that the health-care workers directly administer medicines to patients. This method confirms adherence since the health-care worker observes the patient taking the medicine [39]. This method has been successively used in treating tuberculosis (TB). However, this method cannot be used to assess patient adherence to ART in HIV care

centers due to issues of stigma, confidentiality, identification and the huge cost that will be required for the administering of DOT in such lifelong therapy [40].

b) Patients' self-reports

It is the most usual, feasible, and less expensive method to assess ART adherence. In addition, it has an advantage of easy data collection, and it also help to determine why patients are non-adherence [41]. Patient self-report of taking doses accurately during the past 3 days or the past week is the most practical and readily available tool for the assessment of a patient's adherence in the clinical setting and perhaps the most accurate as only that individual can report his/her actual behavior [42]. Abbreviated forms of questionnaires can be used, even in busy clinics, to quickly assess adherence [43]. Although some patients tend to overestimate their adherence in self report, several literatures have shown that this measure is associated with viral load response [44]. Nevertheless, this method has been criticized for methodological reasons such as reliability, recall bias, social desirability, question style, or the time setting in which the question is asked [45].

c) Pill Counts

It is an objective means of evaluating medicine adherence. It involves physical counting of patient remaining pills by physician, nurse or other health-care practitioner. Pill count adherence is usually calculated by counting the remaining doses of medication and assuming that the remaining pills in excess of what is expected to represent missed doses [46]. Adherence assessed by pill counts correlates better with adherence measured from electronic bottle caps than self-reported dose adherence [47]. However, it has some limitation: when patients remove pills from their containers but do not take them, (i.e. "pill dumping") it leads to overestimation of adherence. In addition, this method does not provide information on other aspects of taking medication, such as dose timing and drug holidays which are important in determining the clinical outcome [48].

d) Pharmacy Refill Data

Pharmacy refill adherence has become an increasingly important measure of adherence to antiretroviral medications [49]. It can serve as an adherence measure by providing the dates on which antiretroviral medications were dispensed. In the event that refills are not obtained in a timely fashion, it is assumed that the patient is not taking medication between refills or is missing doses. It offers a simple, inexpensive, and valid method for measuring adherence [50].

e) Biological Markers

In this method, adherence is monitored by adding secondary non-toxic medicines to indicate the active primary medicine was taken. This has also some challenges like cost involved in its large scale implementation of all classes of ARV [31].

f) Therapeutic drug monitoring (TDM)

TDM involves measuring drug levels in the blood. The ART TDM is useful for the evaluation of non-adherence, multiple drug-food and drug-drug interaction and treatment failure in the absence of viral resistance and non-adherence to medication. TDM is not used routinely to measure adherence because its use is limited to the protease inhibitor classes and also due to cost [33].

g) Medication Event Monitoring System (MEMS)

MEMS contain an electronic chip fitted to pill containers which records the removal of the cap. The chip records the date and time of each opening and closing of the medication bottle. Interpretation of these data assumes that a single dose is taken each time the bottle is opened. It is increasingly being used in resource-limited setting and is reliable in recording dosing histories of patients [33]. The advantage of this method is that it correlates well with virology outcome and data are available in computer accessible format. Limitation of MEMS include

patients opening the bottle but not taking the pill, patients decanting pills, being unavailable for blister packs, measuring only one medication at a time and cost [31].

h) Visual analogue scale (VAS)

It is an inexpensive and valid method of assessing medication adherence. It tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be measured directly. For the measurement of adherence, patients are asked to rate their adherence somewhere along the line from 0 to 10 that best guesses their adherence to the prescribed ART in the past 3 or 4 weeks. It has the potential for use in resource limited setting [31].

i) Pill identification test (PIT)

PIT involves asking the patients to identify the ART pills (they had been prescribed) with “twin pills” that are similar appearing but not identical. PIT is more reliable at the initial phase of treatment and its validity can be correlated with valid self-report adherence measure. On the other hand, it losses the sensitivity in treatment experienced patients [31].

2. STATEMENT OF PURPOSE

Even though the availability of free antiretroviral drugs is increasing, there are still many obstacles that hinder patients to achieve good adherence to antiretroviral therapy. It is estimated that 19% of adult patients are not retained on antiretroviral therapy after 12 months, while for children, 20% are lost after 12 months in poor countries [11]. This will lead to treatment failure and development of drugs resistance mutation not merely at the individual level but consequently at a global level as stated by the WHO “Drug resistance may result in the failure of the immense global and national efforts to provide hope to people living with HIV” [51]. Therefore, it is of necessary to identify and overcome the factors that reduce adherence to antiretroviral therapy for prolonged viral load suppression [41].

In view of the high number of HIV patients taking ART in Kathmandu district and the lack of data surrounding ART adherence in this population, It was necessary to study adherence to ART among HIV-positive population in Kathmandu district and therefore to understand the factors and influencers of adherence to ART.

3. OBJECTIVES

The general objective of this research was to determine the factors that influence adherence to ART among HIV/AIDS patients.

The specific objectives were to:

- Determine the proportion of AIDS patients that adhere to ART.
- Determine socio-demographic and socio-economic factors associated with adherence to ART among HIV/AIDS patients.

4. MATERIALS AND METHODS

4.1 Study area

The Kathmandu district contains six ART centers. This study was conducted at three ART centers located at Sukra Raj Tropical and Infectious disease Hospital (STID), Bir Hospital and Tribhuvan University Teaching Hospital (TUTH) located at Kathmandu district. STID Hospital is the pioneer and largest institution to provide the ART service to HIV patients from all over the country. These hospitals are the main services providers to those who can hardly reach private health institutions and afford the costly services.

4.2 Study period

Study period was from January 2012 to February 2012.

4.3 Study design

Multisite cross-sectional study.

4.4 Sample size

Sample size was calculated using the formula: $n = (4pq/L^2)$ [52, 53].

Where; p = prevalence of ART adherence in Nepal, i.e. 84%, L= Allowable Error, and $q=1-p$.

The value of (p) was taken from a similar study conducted in Nepal previously where the prevalence of adherence was found to be 84% [52]. In the present study, (L) is chosen to be 5% giving a power of $(1-L) = 95\%$.

Therefore the sample size $(N) = 4pq/L^2 = 4 \times 0.84 \times (1-0.84)/(0.05 \times 0.84)^2 = 316$ subjects.

4.5 Inclusion and Exclusion criteria

This study included patients aged 18 years or older who were receiving ART therapy for at least 3 month prior to the study period and were able to give informed consent. Prisoners and patients aged below 18 years old were excluded.

4.6 Study sample

The 316 patients were assessed from the above mentioned three governmental hospitals at Kathmandu district. The three ART centers were selected randomly out of the six centers in the district. The proportion of patients included from each ART center was allocated according to the proportion of patients registered and receiving antiretroviral therapy in each center out of the total number of patients registered and receiving therapy in the three centers combined. Therefore, out of 2240, 102 and 114 patients receiving ART at STID, Bir and TUTH hospitals, respectively, the 316 sample size included 287 (91%), 15 (5%) and 14 (4%) patients from the three hospitals in the same order.

Generally, more than 50 patients used to visit the ART center at STIDH each day, and less number of patients visited the other ART centers. Patients attending outpatient clinics for regular follow-up and to take medicine were approached for interview. Patients were identified with the help of clerks working at the ART centers. They were offered to participate in the study without any incentive.

Eligible patients who were able to give informed consent, were further informed about the purpose, objective and methodology of the study. Then they were interviewed with the help of trained researcher in a private location. Each patient was interviewed for 15-20 minutes. In order to meet the required sample size, the same approach was followed on the patients attending the outpatient clinic during the months of January and February 2012. Pre-ART and ART number of each participant were recorded to prevent any repetition of participants. To avoid information bias, information was obtained only from respondents, and not from health providers.

4.7 Sampling method

Simple random sampling method was used for the research.

4.8 Data collection

The questionnaire (Appendix-1) used in the present study was adapted from an earlier study, with slight modifications, to fit the Nepal's norm [55]. Validity was ensured by careful selection of important items to be included in the questionnaires. In this process, flow of questions, presence of sensitive questions, and appropriateness of categorization of variables were assessed. The questionnaire was finalized by consulting two HIV/AIDS experts in Kathmandu valley and the study supervisor, and then the questionnaire was translated into Nepali (the major language spoken in the Nepal) and verified by a second translator.

The questionnaire consisted of questions covering socio-demographic information related to ART adherence and questions related to the patient's basic characteristics and socioeconomic status. In addition, the patient's medical records were used to collect information about the CD4 cell count and the type of antiretroviral drugs prescribed to them.

The explanatory variables were categorized as follows: age (continuous variable), sex (male/female), education (literate/illiterate), occupation (employed/unemployed), and marital status (unmarried/ ever-married), income (tertiles), and time to reach ART center (continuous variable), use of alcohol in the past month (yes/no), and use of illegal drugs in the past six months preceding the interview (yes/no), reminder method used to take pills (yes/no). The clinical characteristics included the latest available CD4 cell count (≤ 200 / >200), duration of antiretroviral treatment (continuous variable), side effects (yes/no), pills burden (continuous variable).

4.9 Assessment of adherence

The main outcome variable in this analysis was measured by asking patients to recall their intake of prescribed doses in the last seven days prior to the interview. In an attempt to minimize recall bias patients were asked about their adherence over the previous day, previous 3 days and previous week. Self-reported adherence to all ART drugs was calculated

as the ratio of the doses taken during specific time-period over the total number of ART doses prescribed to the same time-period. The result were expressed in percentage and those patients reported intake of 95-100% of the prescribed ART without delay of more than one hour in the past one week were considered adherent to ART. Similarly, those patients who reported taking less than 95% of the prescribed pills were considered as non-adherent.

4.10 Statistical analysis

The information collected from the respondents were sorted, coded and entered in datasheet created in Statistical Package for Social Science (SPSS) version 16. Double data entry system was used to minimize errors in data entry. Differences between adherence and non-adherence subjects were tested using *t*-Student test and Chi-Square test for continuous and categorical explanatory variables, respectively. The strength of association between explanatory variables and adherence was measured using logistic regression and was reported as odds ratio (OR) with 95% confidence interval.

First the association was measured for each explanatory variable in univariate model. Then each univariate model was adjusted for age and sex. In the second step, multivariate analysis was conducted including all the variables in one model. In the last step, only variables with statistical or borderline significant association in the multivariate model (including all variable) were included in the final model. The criterion for statistical significance was $p \leq 0.05$.

5. ETHICAL CONSIDERATION

Ethical approval was obtained from Nepal Health Research Council (NHRC) (Appendix-3) and National Centre for AIDS and STD Control (NCASC). In addition, permission letters were obtained from the directors of the three hospitals. The participants were informed about the aims, methods, and anticipated benefits of the research and they were also assured of their right to terminate their participation at any time if they feel uncomfortable. Both verbal and written informed consent were taken from each participant of the study. The participants were not pressurized or induced to be a subject of research. Moreover to ensure confidentiality and anonymity, participants in the study were numbered consecutively. These numbers were entered into the form thus all study materials like questionnaire did not contain any personal identification.

6. RESULTS

A total of 329 patients were approached and 316 (96%) agreed to sign the informed consent and to participate in this study. Out of the 316 participants, 64.6% (n=201) were men and 35.4% (n=112) were women.

Adherence to ART

The majority of the participants claimed not to have missed a single dose in the past one week, where 86.7% (n=274) reported perfect/good adherence ($\geq 95\%$) and 13.3% (n=42) of the participants reported missing medications during the previous week (Figure 1). The adherence prevalence in men and women was 84.3 % and 91%, respectively (Figure 1).

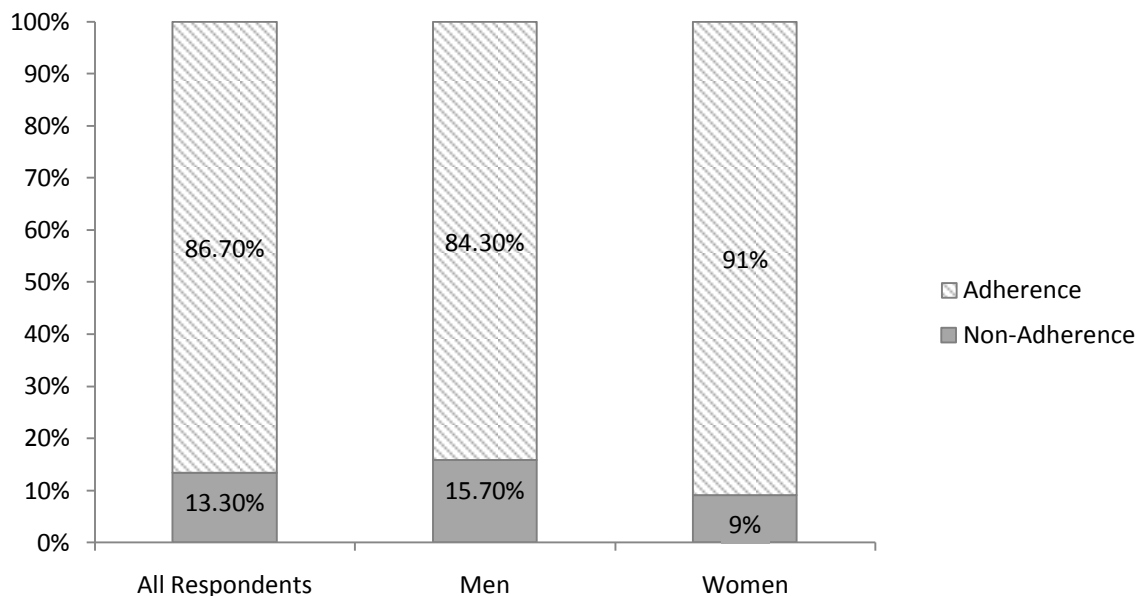


Figure 1: Proportions of HIV/AIDS patients according to antiretroviral therapy adherence status

Patients who reported missing doses in the last week (n=42) were further asked to assess the principal barriers to treatment adherence. The most frequently cited reasons for not taking ART according to the prescribed schedule were “simply forget” and “busy schedule” (Table 3). Around 11% of the participant’s claimed that they were too sick to take prescribed medicine. As a result of stigma, 4.7% respondent missed their doses in order to hide their

status from their family and friends. While, 4.7% patients claimed that they missed their pills due to the side effects.

Table 3: Reasons for missing antiretroviral therapy.

Reasons for missing treatment dose(s)	Frequency (n*)	Percent
Simply forget	34	80%
Busy Schedule	8	19%
Too sick to take medicine	5	11%
Away from home	2	4.7%
Toxicity /side effect	2	4.7%
To hide status	2	4.7%
Loss of medicine	1	2.3%

* Numbers are overlapping (participants could report more than one reason).

At the time of study, all the patients were receiving free ART. Table 2 provides an overview of the ART regimens. Most of the participants (97.4%) were taking the first line standard ART regimens; consists of a combination of 2NRTIs and 1NNRTI (Non/Nucleoside Reverse Transcriptase Inhibitor). Whereas, (AZT, 3tc, NVP) and (AZT, 3tc, EFV) were the two major combination of ART taken by 61% (n=194) and 22.5% (n=71) of participants, respectively. Only 2.5% (n=8) of participants were at second line therapy.

Table 4: Distribution of the participants according to ART regimens.

Participants current ART regimen	Percentage	No of pills /day
AZT,3TC,NVP	61.4%	3
AZT,3TC,EFV	22.5%	4
D4t,3TC,NVP	7%	3
D4,3TC,EFV	6.6%	2
TDF,3TC,EFV	0.6%	4
TDF,3TC,NVP	0.3%	6
AZT,3TC,LPV	0.6%	6
ABC,TDF,LPV	0.3%	5
ABC,DDI,LPV	0.6%	7

General characteristics of the participants:

The mean age was 36.5 years (range 19-56 years), and the majority of the participants were

between 20 and 49 years indicating a reproductive and sexually active sample. The most common mode of infection were heterosexual transmission 76.5% (n=242) and sharing of needle 12% (n=40). While, 6.9% did not know about how they got infected. Minority of individual (3.7%) reported transmission through blood transfusion. Most of the participants (56.6% (n=179)) were from outside the Kathmandu valley. Only 18% (n=56) of the participants were illiterate. The majority of the participants were employed (76.5%), and most of them were farmer. Nevertheless, the levels of poverty were high; median monthly family income of the participants was 6668 Nepalese rupees (NRs) = (75.4US\$), which is below the annual per capita income of Nepali (750 US\$) [56]. Alcohol consumption was reported by 15% (n=48) and illegal drugs use in past 6 months prior to study was reported by 13% (n=43). The mean length of time on ART was 25 months (range 3-61 months). The median CD4 count at start of ART and most recent median CD4 counts were 210 and 299 cells/mm³, respectively. The average length of time to reach the ART center was 2.6 hours (range 1-11 hours) and the average two ways cost to reach ART center was 293NRs. Almost 90% of patients had reported using some kind of medication reminder method to take the medicine at the correct time. Widely used reminder methods were mobile alarm, watch and support from some of the family members. Almost all the patients interviewed were satisfied with their treatment, but many patients had difficulties to come every month to refill ART at ART centers.

Table 5 shows the general characteristics of the study sample by adherence status. Only time to reach the ART center ($p<0.001$), alcohol use ($p=0.026$), illegal drug use ($p=0.017$), side effects ($p=0.005$) and use of reminder method ($p<0.001$) were significantly different by adherence status. Among the participants who took less than 60 minutes to reach the ART center, the prevalence of non-adherence was 7% whereas out of those who took more than 60 minutes, 21% of them were non-adherent to ART. Among the non-alcohol users, only 11%

participants were non-adherent to ART whereas 25% were non-adherent among alcohol users. Similarly, among the illegal drugs users, 37.5% were non-adherent to ART whereas only 9.6% were non-adherent among non-drugs users. Among the participants who did not experience side effects, only 3 % were non-adherent to ART whereas for the participants who experienced side effects, 16.2% were non-adherent to ART. Among the participants who used reminder methods to take the pills, 89% were adherent to ART, whereas 41.1% of the participants who did not use such methods were non-adherent to ART.

Table 5: Socio-demographic and medical characteristics by adherent status

<i>Variables</i>	<i>Total</i>	<i>Adherence</i> <i>N (%)*</i>	<i>Non-Adherence</i> <i>N (%)*</i>	<i>p value</i>
<i>Age (Years)</i>				
18-24	44	41 (93.0)	3 (7.0)	0.270
25-34	87	78 (89.6)	9 (10.4)	
35-49	148	125 (84.4)	23 (15.6)	
>50	37	30 (81.0)	7 (19.0)	
<i>Sex</i>				
Male	204	172 (84.3)	32 (15.6)	0.091
Female	112	102 (91.1)	10 (8.92)	
<i>Marital Status</i>				
Unmarried	68	59 (86.7)	9 (13.3)	0.945
Married	154	135 (87.6)	19 (12.4)	
Divorced	29	25 (86.2)	4 (13.4)	
Widow/Widowers	65	55 (84.6)	10 (15.4)	
<i>Caste</i>				
Brahmin	59	49 (83)	10 (17)	0.614
Chettri	66	60 (90.9)	6 (9.1)	
Dalit	83	71 (85.5)	12 (14.4)	
Janajati	108	94 (87)	14 (13)	
<i>Educational level</i>				
Illiterate	56	48 (85.7)	8 (14.3)	0.848
Primary education	85	71 (83.5)	14 (16.5)	
Secondary education	99	88 (88.8)	11 (11.2)	
Higher secondary	61	54 (88.5)	7 (11.5)	
University Level	15	13 (86.6)	2 (13.4)	

The table continues on the next page.

Table 5 continued

<i>Variables</i>	<i>Total</i>	<i>Adherence</i> <i>N (%)*</i>	<i>Non-Adherence</i> <i>N (%)*</i>	<i>p value</i>
<i>Residence (Region of Kathmandu)</i>				
Inside valley	137	120 (87.5)	17 (12.5)	0.686
Outside valley	179	154 (86)	25 (14)	
<i>Occupation</i>				
Unemployment	71	58 (81.6)	13 (18.4)	0.717
Agriculture	95	83 (87.3)	12 (12.7)	
Labor Work	53	46 (86.7)	7 (13.3)	
Business	68	60 (88.2)	8 (11.8)	
Office work	26	24 (92.3)	2 (7.7)	
Student	3	3 (100)	0 (0)	
<i>Monthly Income</i>				
Lowest tertile	99	83 (83.8)	16 (16.2)	0.054
Middle	107	93 (86.9)	14 (13.1)	
Highest	110	98 (89.1)	12 (10.9)	
<i>Religion</i>				
Hindu	157	141 (89.8)	16 (10.2)	0.375
Buddhist	87	72 (82.7)	14 (17.3)	
Muslim	30	26 (86.6)	4 (13.4)	
Christian	42	34 (80.9)	8 (19.1)	
<i>Family size</i>				
Nuclear	208	158 (75.9)	50 (24.1)	0.746
Joint	115	88 (23.5)	27 (76.5)	
Live alone	92	70 (76.0)	22 (23.0)	
<i>Mode of Transmission</i>				
Heterosexual	242	212 (87.6)	30 (12.3)	0.947
Shared needle	40	34 (85.0)	6 (15.0)	
Blood Transfusion	12	9 (75.0)	3 (25.0)	
Don't Know	22	19 (86.3)	3 (13.7)	
<i>Traveling cost^a</i>				
Lowest tertile	111	103 (92.7)	8 (7.2)	0.054
Middle tertile	99	84 (84.8)	15 (15.2)	
Highest tertile	106	87 (82.0)	19 (18.0)	
<i>Time^b (Minutes)</i>				
≤60	173	161 (93.0)	12 (7.0)	0.000
>60	143	113 (79.0)	30 (21.0)	
<i>Alcohol use^c</i>				
No	268	238 (88.8)	30 (11.2)	0.026
Yes	48	36 (75)	12 (25)	

The table continues on the next page.

Table 5 continued

Variables	Total	<u>Adherence</u> N (%)*	<u>Non-Adherence</u> N (%)*	p value
Illegal Drugs use^d				
Yes	43	27 (62.7)	16 (37.3)	0.017
No	273	247 (90.4)	26 (9.6)	
Reminder method^e				
Yes	287	257 (89.5)	30 (10.5)	0.000
No	29	17 (58.6)	12 (41.4)	
ART Initiation (Month)				
<24	166	148 (89.1)	18 (10.9)	0.178
≥24	150	126 (84.0)	24 (16.0)	
CD4 count^f (cells/mm3)				
<200	56	44 (78.5)	12 (21.6)	0.193
200-350	148	130 (87.8)	18 (12.2)	
>350	99	87 (87.8)	12 (12.2)	
Side effect				
Yes	248	208 (83.8)	40 (16.2)	0.005
No	68	66 (97.0)	2 (3.0)	
Tablets daily^g				
≤ 3	237	202 (85.3)	35 (14.7)	0.180
>3	79	72 (91.1)	7 (8.9)	

* Row percentage

^a Traveling cost: cost to reach ART center.

^b Time: Total time to reach ART center.

^c Reminder method: using of any reminder tool to take ART.

^d Alcohol use:n Alcohol use in past 1 month.

^e Illegal drugs use: Illegal drugs use in past 6 month prior to study.

^f CD4 count : Latest available CD4 cell count.

^g Tablets daily: Numbers of Tablets taken per day.

Table 6 presents the characteristics of study population stratified by gender. Only, time to reach ART center, history of illegal drugs use in the past 6 month, not using of reminder methods were significantly different by adherence status among both genders. While, alcohol use and side effects were only significantly different among men. Among the past alcohol user the prevalence of non-adherence to ART was doubled for men (31.1%) compared to women (15.8%). Among the past illegal drugs users the prevalence of non-adherence was 40% in men and 30% in women. The prevalence of non-adherence among men who had

experienced side effects was almost double (19.9%) compared to women (9.8 %). Among those who used reminder methods to take the ART, the prevalence of adherence was 87.2 % in men and 94.1% in women.

Table 6: Characteristics of study participants by sex and adherence status.

	Men			Women		
	Adherence N (%)	Non- adherence N (%)	<i>p</i> value	Adherence N (%)	Non- adherence N (%)	<i>p</i> value
Age*	36.34 (9.3)	38.4(8.7)	0.388	35.7(9.2)	41(5.9)	0.190
Marital Status						
Unmarried	37 (86)	6 (14)	0.492	22 (88)	3 (12)	0.541
Ever married	135 (83.8)	26 (16.2)		80 (91.9)	7 (8.1)	
Education status						
Illiterate	27 (84.3)	5 (15.7)	0.992	81 (92)	7 (8)	0.489
Literate	147 (85.4)	27 (14.6)		21 (87.5)	3 (12.5)	
Residence						
Inside valley	76 (83.5)	15 (16.5)	0.779	44 (95.6)	8 (4.4)	0.156
Outside valley	96 (84.9)	17 (15.1)		58 (87.8)	8 (12.2)	
Occupation						
Employed	137 (85.6)	23 (14.4)	0.326	76 (92.6)	6 (7.4)	0.323
Unemployed	35 (79.5)	9 (20.5)		26 (86.6)	4 (13.4)	
Monthly Income						
Lower tertile	52 (83.8)	10 (16.2)	0.623	31 (83.7)	6 (16.3)	0.160
Middle tertile	52 (81.2)	12 (18.8)		41 (95.3)	2 (4.7)	
Higher tertile	68 (87.1)	10 (12.9)		30 (93.7)	2(6.3)	
Family size						
Single	45 (83.3)	9 (16.7)	0.817	88 (91.6)	8 (8.4)	0.588
Joint	127(84.6)	23(15.4)		14 (87.5)	2 (12.5)	
Traveling cost						
Lower quartile	63 (92.6)	6 (7.4)	0.114	40 (95.2)	2 (4.8)	0.471
Middle quartile	58 (82.8)	12 (17.2)		26 (89.6)	3 (10.4)	
Higher quartile	51(78.4)	14 (21.6)		36 (87.8)	5 (12.2)	
Time	2.45 (1.5)	3.1 (1.7)	0.012	2.6 (1.6)	4.4 (2.7)	0.014
Alcohol use						
Yes	20 (68.9)	9 (31.1)	0.014	16 (84.2)	3 (15.8)	0.250
No	152 (86.8)	23 (13.2)		86 (92.4)	7 (7.6)	
Illegal Drugs						
Yes	20 (60)	13 (40)	0.000	7 (70)	3 (30)	0.014
No	152 (88.8)	19 (11.2)		95 (95.9)	7 (4.1)	
Reminders Method						
Yes	160 (87.2)	24 (12.8)	0.002	97 (94.1)	6 (5.9)	0.000
No	12 (60)	8 (40)		5 (56)	4 (44)	

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Table 6 continued

	Men			Women		
	Adherence N (%)	Non- adherence N (%)	<i>p</i> value	Adherence N (%)	Non- adherence N (%)	<i>p</i> value
ART Initiation						
(Month)						
<24	92 (85.9)	15 (14.1)	0.492	56 (94.9)	3 (5.1)	0.132
≥24	80 (82.4)	17 (17.6)		46 (86.7)	7 (13.3)	
CD4 count						
(cells/mm³)						
≤200	27 (75)	9 (25)	0.115	20 (86.3)	3 (13.7)	0.503
>200	138 (85.7)	23 (14.3)		76 (91.5)	7 (8.5)	
Side effect						
Yes	125 (80.1)	31 (19.9)	0.003	83 (90.2)	9 (9.8)	0.497
No	47 (97.9)	1 (2.1)		19 (95)	1 (5)	
Tablets daily						
≤ 3	131 (83.4)	26 (16.6)	0.180	71 (88.7)	9 (11.3)	0.173
>3	41 (87.2)	6 (12.8)		31 (96)	1 (4)	

* Mean (SD)

A total of 248 (78.5%) participants reported experiencing side effect with their medication in the past months. However, only 4.7% of them considered the side effects as barrier to ART adherence. Different side effects reported by participants are shown in Table 7.

Table 7: Distribution of the self-reported side effects of antiretroviral therapy.

Side Effect	N*(%)	P-value
Itching	72 (22.8%)	0.433
Headache	43 (13.6)	0.395
Dizziness	40 (12.7%)	0.002
Skin rash	39 (12.3%)	0.000
Vomiting	39 (12.3%)	0.008
Fatigue	34 (10.8%)	0.838
Prolonged fever	32 (10.1%)	0.185
Arthritis	23(7.3%)	0.500
Persistent Cough	17 (5.4%)	0.438
Anemia	16(5.1%)	0.395
Pain and numbness	15(4.7%)	0.433
Diarrhoea	10(3.2%)	0.525
Others	13 (4.1%)	0.725
Insomnia	9 (2.8%)	0.845

* Number are overlapping (participants could report more than one reasons)

The most commonly reported side effects were skin itching (22.8%); headache (13.6%); dizziness (12.7%). These side effects were significantly more reported among non-adherent patients ($p<0.005$).

Eight participants reported that they stopped taking the ART at least once since they began the treatment. Different reasons given for stopping their ART are shown in Table 8.

Table 8: Reasons reported for temporal stopping of ART

Reason	N	Percentage
Inefficient treatment	2	25%
Side effects	2	25%
Financial difficulty	2	25%
Inconvenience to visit ART center	2	25%
Total	8	100%

Predictors of antiretroviral therapy non-adherence

Table 9 presents the crude and adjusted odds ratios of non-adherence by different predictors. In univariate analysis, non-adherence was significantly associated with the time taken to reach the ART center, past alcohol use, past illegal drugs use, side effects, lowest tertile of traveling cost to ART center and no use of reminder methods. A borderline association was observed with age.

After, controlling (adjusting) for age and sex the same variables as in univariate analysis were significantly associated with non-adherence ($p<0.05$) and the adjusted odds ratio were almost unchanged; lowest quartile of traveling cost to ART center (OR 0.33 95% CI 0.14-0.82), time taken to reach the ART center (OR 1.39; 95% CI 1.16-1.67), alcohol use in past one month (OR 2.76; 95% CI 1.27-5.96), past use of illegal drugs (OR 5.29; 95% CI 2.49-11.24), side effect (OR 6.99; 95% CI 1.63-29.98), and use of reminder methods (OR 6.04; 95% CI 2.59-14.09) (Table 9).

Table 9: Risk factors for non-adherence (univariate and age- & sex-adjusted)

Variables	Crude OR (95% CI)	Age & sex adjusted OR (95% CI)
Age	1.03 (1.0-1.07)	1.03 (0.99-1.07)
Sex		
Male	1.89 (0.89-4.02)	1.87 (0.88-3.99)
Female	1	
Marital Status		
Ever married	1.00 (0.45-2.22)	0.62 (0.24-1.54)
Unmarried	1	
Education status		
Illiterate	1.10(0.48-2.54)	1.23 (0.52-2.86)
Literate	1	
Occupation		
Unemployed	1.56 (0.76-3.19)	1.68 (0.81-3.47)
Employed	1	
Income		
Lower quartile	1.57 (0.70-3.51)	1.81 (0.79-4.10)
Middle quartile	1.22 (0.54-2.79)	1.32 (0.57-3.04)
Higher quartile	1	
Family		
Without family	1.29 (0.61-2.72)	1.11(0.52-2.38)
With family	1	
Traveling cost		
Lower quartile	0.35 (0.14-0.85)	0.33 (0.14-0.82)
Middle quartile	0.81 (0.39-1.71)	0.73 (0.34-1.57)
Higher quartile	1	
Time	1.34 (1.13-1.61)	1.39 (1.16-1.67)
Alcohol use		
Yes	2.64 (1.24-5.63)	2.76 (1.27-5.96)
No	1	
Illegal Drugs use		
Yes	5.6 (2.68-11.78)	5.29 (2.49-11.24)
No	1	
Reminders use		
Yes	1	
No	6.04 (2.63-13.86)	6.04(2.59-14.09)
ART Initiation (Month)		
<24	1	
≥24	1.56 (0.81-3.01)	1.24 (0.60-2.57)
CD4 count (cells/mm3)		
≤200	1.82 (0.86-3.81)	1.89 (0.89-4.01)
>200	1	
Side effect		
Yes	6.34 (1.49-26.97)	6.99 (1.63-29.98)
No	1	
Tablets daily	0.97 (0.59-1.59)	0.96 (0.59-1.56)

When compared by gender, it is interesting that in contrast to women, men with a history of alcohol use in past month (OR 2.9; CI 1.20-7.31) and those who experienced side effects of ART (OR 11.65; CI 1.54-87.5) have shown statistical significant association with non-adherence. In other words, male respondents who had history of alcohol use in the past one month were 2.9 times more likely to report non-adherence than those who didn't report alcohol use. Similarly, the odds of non-adherence in men who experienced side effects in the past months increased by 1065% compared to men who didn't experience any side effect.

In multivariate analysis including all the variables listed in Table 9; only, age ($p=0.025$), sex ($p=0.029$), time taken to reach the ART center ($p=0.055$), history of past drug use ($p=0.003$), side effects, ($p=0.012$) and no use of reminder method ($p=0.018$) were independently associated with non-adherence. A borderline association was observed with the alcohol use in past one month and non-adherence ($p=0.092$).

The final model included age, sex, time taken to reach ART center, past illegal drugs use, past alcohol use, side effects, and use of reminder tools (Table 10). Negative trends for medication adherence were seen for advancing age. Increment in age by one year increased the risk of non-adherence by 4% (OR 1.04; 95% CI 1.00-1.09). Increase of the traveling time to ART center by one hour was associated with 38% increase in the risk of being non-adherent (OR 1.38; 95% CI 1.12-1.71). The upper limit of the confidence interval for this odds ratio shows that this increased odd could be as much as 71%.

There was no interaction effect seen between the use of alcohol and illegal drugs. However, in the final model, although the odds of non-adherence was more than double in patients with history of alcohol use, the association did not reach a statistically significant level (OR 2.26; 95% CI 0.93-5.44). On the other hand, patients with history of illegal drugs use had almost 4 times the odds of being non-adherent than patients without history of illegal drugs use (OR 3.98; 95% CI 1.71-9.24). The odds of non-adherence increased 388% in patients who had side

effects (OR 4.88; 95% CI 1.09-21.8). Patients who had used reminder tools to take the medication were 3.45 times more likely to adhere to ART compared to those who did not use any reminder tools (OR 3.45; 95% CI 1.33-8.91).

Table 10: Risk factors for non-adherence (final multivariate model)

Variables	Adherence/ Non-adherence	Crude OR (95% CI)	<i>p</i>-value	Adjusted OR (95% CI)	<i>p</i>-value
Age		1.03 (1.00-1.07)	0.053	1.04(1.00-1.09)	0.048
Sex					
Male	172/32	1.88 (0.89-4.02)	0.459	2.19 (0.92-5.25)	0.076
Female	102/10	1			
Time		1.34 (1.13-1.61)	0.001	1.38 (1.12-1.71)	0.002
Alcohol use					
Yes	30/12	2.64 (1.24-5.63)	0.012	2.26 (0.93-5.44)	0.069
No	238/36	1			
Illegal drugs use					
Yes	27/16	5.6 (2.68-11.78)	0.000	3.98 (1.71-9.24)	0.001
No	247/26	1			
Side effect					
Yes	208/40	6.34 (1.49-26.97)	0.012	4.88 (1.09-21.8)	0.038
No	66/2	1			
Reminder use					
Yes	257/17	1			
No	30/12	6.04 (2.63-13.86)	0.000	3.45 (1.33-8.91)	0.010

7. DISCUSSION

The overall self-reported adherence rate for one week was 86.7%. The results show that factors such as age, time taken to reach ART center, past drug use, side effects and not using reminder tools are independently associated with non-adherence.

The main reasons accounted for non-adherence were patients simply forgetting to take ART and having a busy schedule and this finding correlates with the finding of other studies [53,54,57,58]. In fact, due to variation in measurement methods of adherence, it is difficult to compare findings from different studies. However, the literature shows that the developing countries have better adherence rates than developed countries. For example, countries like Uganda (89%), Kenya (82%) showed better adherence rates [44,57]. On the contrary, countries like the United States (50%), France (29.1%), and Brazil (63.1%) have lower adherence rates [42].

In this study the level of adherence to antiretroviral therapy, is slightly higher, and consistent to other similar studies in Nepal and compatible to several other studies conducted in developing countries which were also based on self-reported adherence [54,59,60,61]. The possible explanation for getting higher adherence in this study might be due to using self-reported adherence, only assessing the adherence of one week and selecting participants through out-patient department/clinic (OPD) which may have resulted in the participation of only active people. However, results of this study are unique because to my knowledge, this is the first study to assess the factors associated with adherence to ART among HIV patients in Kathmandu district and the first to examine adherence among patients who are receiving free ART services at government hospitals.

Determinants of ART adherence

a) Gender

The proportion of men in this study was approximately two-fold that of women and is similar to the proportion of HIV& AIDS reported in Nepal [23]. The higher number of male respondents might be due to women being far less likely to come forward for treatment. In the univariate analysis, male gender was associated with non-adherence to ART. This might be related to the limitation of cross-sectional-study. However, in multivariate analysis gender was not a significant predictor of adherence. The finding is in agreement with studies elsewhere [52,57,61] but in contrast with the finding of Wasti *et al* in Nepal [54]. In that mixed method study, it has been reported that the HIV infected women are less likely to adhere to ART, more prone to discrimination by others and tend to be more highly stigmatized than men. Furthermore, in most of the developing countries, the HIV positive women pose a number of challenges regarding social barriers, psychological, epidemiologic, economic and biological aspects, which impact their ability to take medication. So, the challenge to improve access and adherence to ART in women remains critical in most of developing countries.

b) Age

This study shows that ART adherence varied significantly by age. Increase in age by one year increases the risk of being non-adherent by 4%. Increased risk of non-adherent with increasing age might be due to alternation in life style and having a busy schedule with increase in age. This finding contrasts with the American study by Barclay *et al* showing the patients aged less than 50 years were 2 times more likely to non-adhere [62] and differs from some studies showing no association between age and adherence [54,59,58]. Such variation in results could be due to differences between studies in terms of sampling population. Generally, due to antiretroviral therapy, the number of persons aged 50 years and older living

with HIV& AIDS is increasing [63]. Therefore, further studies on risk associated with old age are needed.

c) Traveling cost and Time

Significant interaction between traveling cost and time taken to reach ART center was found. While traveling cost showed non-significant association in the multivariate model, time continued to have significant independent association with non-adherence; the odds non-adherence increased by 40% for each one extra hour taken to reach ART center. This could imply that the effect of traveling cost is explained within the time taken to reach the ART center. Moreover, the latter could also embrace other daily activities affecting the patients' plans or priorities according to time available every day. In addition, few patients cited stopping the medicine in past due to the various cost associated with treatment.

Overall, the results of this study provide evidence that lack of access due to time to reach ART center can hinder the improvement of adherence among ART patients in resource-limited countries. In accordance to this, two Indian studies [53, 61] and two African studies [57,58] showed that travelling from distant places to ART centres was one of the barriers for adherence to ART. It is unfortunate that, despite extension of ART centers in different regions, PLWH were unwilling to seek treatments at the nearest health institution because of fear of stigmatization [59]. In such situation, patients may have to travel long distances to seek ART services where time could be a problem. In Nepal, traveling long distances to receive treatment was common, and not surprisingly, transportation difficulties were often reported to be a major hindrance to adherence [60].

d) Side effects

This study shows that patients' experience of medical side effects predicted non-adherence. Side effects such as dizziness, skin rash, vomiting were more frequently reported. The odds of adherence among those who didn't experience side effects was 4.88 times higher than those

who reported experiencing medication side effects. This finding was consistent with findings of several other studies [54,58,59,64]. In addition, one Meta-analysis showed that varying from mild to severe and from acute to chronic, side effects and toxicity of the complex ART drugs was an important reason for non-adherence [65]. However, one Kenyan study showed that adverse side effects doesn't significantly influence non-adherence [57]. So it is important to educate and counsel patients on how to cope with these side effects. As mentioned in systematic review by wasti *et al* "Trust in ART medication, self-awareness of one's health and knowledge of the consequences of adherence and non-adherence are an important basis for trust and belief that can reinforce adherence despite side effect" [60]. Symptoms management is a vital part of successful adherence to ART. Hence, it is necessary to discuss all potential side effects with the patients before they begin the medications to prevent feelings of premeditated non-disclosure. Moreover, each patient must be assessed individually for readiness to adhere to a complex medication regimen [33].

e) Illegal drugs use

Both illegal drugs use and alcohol use were associated with non-adherence in univariate analysis and illegal drugs use remained the strongest predictor for non-adherence in multivariate analysis. Among men, only alcohol use was associated with worse adherence. Alcohol use was not associated with worsened adherence in women in final multivariate model. This result shows that alcohol use may disproportionately impact antiretroviral adherence in men. In a Meta analysis, alcohol use was associated with 40% to 50% reduction of adherence [65]. Therefore, more focused interventions for enhancing adherence are needed among alcohol user men. Similarly, the odds of non-adherence among those who had past history of illegal drugs use was 4 times higher than those who did not report history of past illegal drugs use. This finding was in agreement with other studies [60,66,67,68]. Other studies showed that patients with history of substance use were significantly less engaged

with their health care provider and such patients are likely to exhibit higher rate of refusal to treatment [32,65]. Furthermore, neurological and psychological problems can yet be additional factors related to non-adherence among illegal drug users.

f) Reminder tools use

Both univariate and multivariate analysis in this study confirmed that having a reminder tool is a strong predictor of adherence. This finding is supported by Wang *et al* who found that the risk of non-adherence among patients with no reminder tool was 4.2 times greater than for those who employed some reminder method [29]. Edward *et al.* in a review on adherence of ART in developing and developed countries showed that support from friends and family as reminders facilitates successful adherence to ART [69]. In addition, disclosing one's ART status to others had positive influence on adherence [60,65].

Although, many other potential predictors were included in this study, they did not show consistent associations with the adherence of ART.

The number of pills taken per day was not associated with the adherence in both univariate and multivariate analysis. However, several other studies have shown that adherence decreases with increase in the number of tablets and number of daily doses [42,61]. One Indian cohort study showed that medication adherence increased by 100% in those on less than 5 tablets per day [61]. In contrast to this, various studies reported that despite having the new regimens- fewer tablets and daily doses-, adherence still remains a problem [28,42]. Due to the small sample size of this cross-sectional study and the adherence assessment over a short period of time, it is difficult to reach valid conclusions on whether the number of tablet per day is associated with ART adherence or not. Thus, other objective tools such as pill count, electronic pill caps, and other biological methods should be included in future studies.

Interestingly, no significant associations were found between levels of education and income and adherence. This is in accordance to other studies on adherence in Nepal where the

reported income and education level did not significantly influence non-adherence. [54,59] Similarly, marital status did not significantly influence adherence in this study. This finding is inconsistent with the findings of Byakika *et al* in Uganda. [70] In relation to the time elapse since the start of the antiretroviral treatment, in this study being on ART for less than 2 year or more than 2 year was not associated with non-adherence. This differs from literature, which was consistent with finding of other several studies [42,53,58] but this is in contrast with the finding of Indian cohort study by Cauldbeck *et al*. [61] who found that duration of treatment for less than 6 months or greater than 10 years was associated with the largest number of missed doses.

8. Strength and Limitation

The cross-sectional design made it faster, cheaper and easier to perform the study. In order to ensure the validity, a questionnaire used earlier in a study in Togo was used. Additionally, in order to ascertain the level of understanding of questionnaires, a small pilot test was conducted among few HIV& AIDS patients. Patients were interviewed from ART centers at three government hospitals so they can be considered as a representative of HIV& AIDS patients in Nepal. Also, the sample size in this study is higher than previous similar studies conducted in Nepal. In order to minimize the selection bias, all patients coming to out-patients department in the month of January and February were approached for interview and the response rate was high. Adherence was assessed only for one week prior to the study so that patients can accurately recall their behavior minimizing the chances of recall bias. Furthermore, multivariate modeling was used to assess the factor associated with adherence. Despite the numerous strengths, this study has some limitations. Adherence was assessed only in terms of missing doses. Other dimensions of adherence such as whether patients took medicine in accordance to time and dietary instructions were not interviewed. Although,

selection bias is limited in this study, it should be mentioned that only patients who personally collected/refilled their treatment from the ART centers were included and no approach was made to patients having their ART delivered at home by volunteers. On the other hand, there might be other confounding factors that were not measured and adjusted for in this study, and the patients' self-reports might have been touched by the social desirability effect. Furthermore, this study is cross-sectional; therefore, the temporal relationship among variables studied is unknown, thus the causal relation cannot be established.

9. CONCLUSION

Prevalence of adherence found in this study seems to be encouraging. The finding suggests that male gender, age, time taken to reach ART center, side effects and substance use present additional barrier for adherence to ART. Whereas having reminder tools to take the pills enhanced adherence. Nevertheless, even within the context where free ART service is provided to HIV patients, time taken to reach the ART center remains an important barrier to access and adherence to HIV patients. Moreover, current finding demonstrates that in spite of universal access to ART, achieving perfect adherence remains a challenge with HIV& AIDS and non-adherence remains a barrier to combat the epidemic. In order to improve adherence among HIV patients, NCASC should provide equitable access to its services regardless of gender or socioeconomic status of the patients. Adherence to ART varies over time and between individuals. Therefore using multiple measures, further longitudinal research including both public and private services delivery sites are needs to assess to determine the factors associated with adherence.

10. RECOMMENDATIONS

- Addressing non-adherence to ART in developing countries like Nepal may require different solution from those in developed countries, where access to ART is not a major concern.
- In an effort to remove obstacles to treatment adherence, health care providers should give clear instructions and proper counseling to patients focusing on managing side effects. Besides that, prescribing greatly simplified ART regimen that has low incidence and severity of adverse effects can improve adherence.
- To improve adherence it is important to empower patients by providing skills to take medicines in public places, where they might have to hide to take medicine due to other socio-cultural obligation. In addition, governments should encourage a supportive environment where PLWHs do not have to worry about stigma and discrimination.
- Maintaining morning and evening OPDs or keeping ART centre staff on shift duties can help the patients to better manage their time. In this case, patients can manage time to come to ART center despite having busy schedule.
- Different electronic reminder devices such as watch, mobile, pillboxes with alarms should be widely developed as a part of the set of HIV treatment adherence tools.
- Patients reporting a history of illicit drug use should be targeted to enhance adherence to ART.
- To encourage patients to adhere to their medication, community support such as Community Care Centers (CCCs), Comprehensive care center and home-based care need to expand at village or districts/regions which have high levels of PLWH.

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71. APPENDICES

Appendix 1: Data collection form (questionnaire)

Participant number:

ART Site.....

नमस्कार !

म राजेश सिखेल स्वास्थ्यको विद्यार्थी हुँ। अहिले म ART नियमितताका बारेमा अध्ययन गरिरहेको छु। यस अध्ययनमा तपाईंहरूको सहभागीताको अपेक्षा राख्छु। तपाईंले दिनुभएका सूचनाहरूले ART नियमित प्रयोग गर्नका निम्ति आइपुग्ने अप्ठ्याराहरूका बारेमा जानकारी दिनेछ, र स्वास्थ्य सेवामा टेवा पुग्नेछ।

यो प्रश्नावली जम्मा १०-२० मिनेट सम्मको हुनेछ र तपाईंले दिएको सूचनालाई गोप्य राखिने छ। तपाईं यस प्रश्नावलीमा बिना करकाप भाग लिन सक्नुहुनेछ। भाग लिनु भएमा तपाईंका विचारहरू अमूल्य हुनेछन्।

यदी तपाईंलाई यस अध्ययनका बारेमा केही जिज्ञासा छ भने निर्धक्क मलाई सोध्न सक्नुहुनेछ।

के म अब तपाईंलाई प्रश्न गर्न सक्छु ?

.....
हस्ताक्षर:

ART नियमितता सम्बन्धी प्रश्नावली

१. उमेर
२. लिंग:
(१) पुरुष, (२) महिला, (३) तेस्रो लिंगी
३. वैवाहिक अवस्था:
(१) विवाहित, (२) अविवाहित, (३) सम्बन्ध बिच्छेद, (४) विधवा, (५) विधुर
४. जात:
(१) ब्राह्मण, (२) क्षेत्री, (३) दलित, (४) अन्य
५. धर्म:
(१) हिन्दू, (२) बौद्ध, (३) मुस्लिम, (४) क्रिस्चियन (५) अन्य
६. तपाईंको शैक्षिक योग्यता कति छ ?
(१) साक्षर (२) निरक्षर, (३) प्राथमिक शिक्षा (४) माध्यमिक शिक्षा (५) उच्च माध्यमिक शिक्षा (६) व्यवसायिक शिक्षा (७) विश्वविद्यालय शिक्षा
७. पेशा:
(१) बेरोजगार, (२) कृषि (३) श्रमिक (४) व्यापार (५) अफिसको काम/ सेवा (६) अन्य
८. तपाईंको मासिक पारिवारिक आयदानी कति छ ?
.....
९. तपाईंको बासस्थान
(१) काठमाडौं उपत्यका भित्र (२) उपत्यका बाहिर
१०. पारिवारिक अवस्था
(१) एकल (२) सपुत्र
११. ART केन्द्रमा जानका लागि यातायातको सुविधा

(१) बस (२) पैत्रल (३) अन्य

१२. ART केन्द्रमा अड्डनका लागि लाग्ने दोहोरो भाडा

१३. ART केन्द्रमा पुग्नुका लागि लाग्ने समय

१४. एच आइभी बाट कसरी संक्रमित हुनुभएको हो ?

(१) विपरित लिङ्गीसँगको सम्बन्ध (२) समलिङ्गीसँगको सम्बन्ध (३) एउटै सुईको प्रयोग
(४) रगत लिँदा (५) अन्य कुनै (६) थाहा भएन

१५. तपाईं आफू एच.आइ.भी एड्सबाट संक्रमित हुनुभएको कहिले थाहा पाउनु भयो ?
महिना..... साल

१६. तपाईंले कहिले देखि ART सुरु गर्नुभयो ?
महिना साल

१७. के तपाईं अघोरोगबाट संक्रमित हुनुहुन्छ ?

(१) छु (२) छैन (३) थाहा छैन

१८. ART को भूमिकाबारे तपाईंलाई केही थाहा छ ?

(१) छ (२) छैन

१९. के यो संयुक्त उपचार पद्धति हो ?

(१) हो (२) होइन

तपाईंले प्रयोग गरिरहनु भएको औषधिको बारेमा मलाई केही भन्न सक्नुहुन्छ ?

२०. तपाईंले प्रयोग गरिरहनु भएको औषधिको बारेमा तपाईंलाई जानकारी छ ?
(१) छ (२) छैन

तपाईंलाई सेवन गर्ने भनिएका औषधि के हुन् ?

२१. औषधि खाने समय

(१) खाना पहिले (२) खाना पछि (३) कुनै समय छैन

२२. औषधि सेवन गर्ने समयका लागि सफुन्ने तरिका केही अपनाउनु भएको छ ?

(१) छ (२) छैन

२३. यदी छ भने के अपनाउनु भएको छ ?

(१) घडी (२) परिवारका सदस्यको सहयोग (३) अन्य

उपचारको अवलोकन:

२४. विगत ७ दिनमा तपाईंले कुनै औषधि दिन विर्सनु भएको छ ?
(१) छ (२) छैन

२५. छ भने कति पटक ?

२६. विगत ७ दिनमा तपाईंले कति Tablet बिनु भएको छैन ?

२७. तपाईंलाई १ हप्ताको लागि कति Tablet सेवन गर्न भनिएको थियो ?

२८. तपाईंलाई औषधिको नियमित प्रयोग नगर्दा हुने हार्दा नोक्सानीका बारेमा केही जानकारी छ अथवा कसैले सल्लाह दिएको छ ?

(१) छ (२) छैन

२९. यदि छ भने कसले ?
(१) कन्सल्टेन्ट (२) डाक्टर (३) अभिभावक (४) साथी

औषधि सेवनमा अनियमितता हुनुका कारणहरू:

३०. तपाईंले औषधि नियमित प्रयोग नगर्नुका कारणहरू केही छन् ?
(१) छ (२) छैन

यदि छ भने के हुन् ?

३१. तपाईंलाई औषधि सेवनबाट कुनै अप्ठ्याराहरू आएका छन् ?
(१) छ (२) छैन
यदि छ भने ती के हुन् ?

३२. के तपाईंले कुनै कारणबाट औषधि सेवन गर्न छोड्नु भएको छ ? अथवा औषधि सेवनमा परिवर्तन गर्नु भएको छ ?
(१) छ (२) छैन

३३. यदि छ भने भने ती कारणहरू के हुन् त ? (१) भन्दा बढीमा टिक लगाउन सक्नु हुनेछ।
(१) औषधिको प्रभावको कमी
(२) Side Effect हो, होइन
(३) मलाई उपचारलाई नियमितता दिनु छैन
(४) ART सेन्टरमा औषधिको कमी
(५) अन्य

३४. विगतका महिनाहरूमा तपाईं मध्यमन गर्नुहुन्थ्यो ?
(१) यसको सेवन कहिल्यै गरेको छैन
(२) महिनाको १ पटक
(३) महिनाको २, ३ पटक
(४) हप्तामा १, २ पटक
(५) हप्तामा ३, ४ पटक
(६) हप्ताको प्रत्येक दिन जसो
(७) दैनिक

३५. के तपाईं लागू पदार्थको सेवन गर्नुहुन्थ्यो ?
(१) पहिला गर्ने गर्थे
(२) दैनिक गर्ने गर्छु
(३) कहिलेकाहीँ गर्ने गर्छु
(४) यसको सेवन कहिल्यै गरेको छैन

३६. लागू पदार्थको प्रयोग सिस्टिमद्वारा गर्नु भएको छ ?
(१) छ (२) छैन

३७. यदि पहिले गर्नुभएको छ भने आजभोली प्रयोग गर्नु हुन्छ कि हुन्न ?
(१) गर्छु (२) गर्दिन

३८. के तपाईं आफ्नो उपचारबाट सन्तुष्ट हुनुहुन्छ ?
(१) छु (२) छैन

३९. यदि हुनुहुन्न भने के कारणले

यस प्रस्तावलीमा सहभागी भई सहयोग गर्नु भएकोमा आभार व्यक्त गर्दछु ।

मेडिकल रजिष्टरबाट संकलित तथ्यहरू
सक्रामित व्यक्तिको हालको CD4 cell संख्या
सक्रामित व्यक्तिले नियमित सेवन गरिरहेको औषधि

(English translation)

ART No

ART site:.....

INFORMED CONSENT

Hello. My name is Rajesh Shigdel and I am Masters Student of Public health. I am conducting a survey about adherence of ART . I will appreciate your participation in this survey. The information you provide will help to know the factor affecting the Adherence to ART and help to plan health services. The survey usually takes between 10 and 20 minutes to complete. Whatever information you provide will be kept strictly confidential and will not be shown to other persons.

Participation in this survey is voluntary and you can choose not to answer any individual question or all of the questions. However, I hope that you will participate in this survey since your views are important.

At this time, do you want to ask me anything about the survey?

Are you willing to participate in the study?

1. Yes 2. No

Signature.....

Questionnaire for assessing adherence level to antiretroviral therapy among HIV/AIDS patients:

I. Socio-demographic characteristics

1. Age:

2. Sex: 1= male 2= female 3 .Third gender

3. Marital Status: 1. Married 2. Unmarried. 3. Divorce. 4. Widow/widower. 5.Co-habiting

4. Caste: 1. Brahmin 2.chettri 3.Dalit 4.Janajati

5. Religion: 1. Hindu 2.Buddhist 3.Muslim 4.Christian 5. Other

6. What education do you have?

1. Illiterate. If literate: 2. Primary education. 3. Secondary education. 4. Vocational education.

5. Higher secondary education 6. University level

7. Occupation: 1. unemployment 2. Agriculture. 3. Labour worker. 4. Business.

5. Office worker 6. Others.....

8. Place of residence: 1. Inside Kathmandu Valley 2. Outside Kathmandu valley

9. Family size: 1. Nuclear. 2. Joint. 3. Live alone.

10. Monthly family income

11. Means of transportation to ART center? 1. By Bus 2.By foot 3. Other

12. Cost of traveling to ART center?

13. Time to reach at ART Center: Minutes

14. How were you infected with HIV?

1. Heterosexual intercourse (Vaginal Intercourse)... 2. Homosexual intercourse (anal intercourse).....

3. Shared needles 4. Blood transform.....

5. Other..... 6. Don't know

15. When have you been diagnosed as positive for HIV? Month /___/___/ Year /___/___/___/___/

16. When did you start on the ART? Month /___/___/ Year /___/___/___/___/

II. Knowledge of the treatment

17. Do you know the role of ART? 1=Yes 2=No

18. Is it a combination treatment? 1=Yes 2=No

Would you give me some information about the medicament you are taking?

19. Do you know the ART's medicine prescribed to you? 1=Yes 2=No

20. Type of antiretroviral medication prescribed to you:

REMARK: Taking according to the meal:

1=Before 2=During 3=After 4= No particular recommendation

21. Do you have own method to remember time and recommendation to take your medicine?

1= Yes 2=No

22. If yes, which one? 1= Watch ... 2=one of my family's member 3=other.....

III. ADHERENCE OF THE TREATMENT

23. During the last seven (07) Days have you missed to take your medicament? 1=Yes 2=No

24. How many time(s)?

25. How many tablets are not taken?

26. How many tablets were prescribed per day?

27. Have you at least once got some information (advices) about the consequences of a bad using of your treatment? Yes / No

28. If yes, from whom? 1= Consultant/ (Adviser) 2= Doctor 3= Parents 4=Friends

IV. FACTORS OF POOR ADHERENCE

29. Is there any reason behind that you are not taking medicine regularly? Yes / No

If yes: then can you mention the reason

V. SIDE EFFECTS

30. Have you any undesirable or sides effects during your treatment? 1=Yes 2=No

If yes, what are those side effect

31. Have you ever stopped or changed the medicaments? 1=Yes 2=No

32. If yes, Why? You can tick more than one answer.

1. Inefficiency treatment ... 2.sides effects.... 3.financial difficulty.....

4. I didn't want to continue treatment 5.Lack of drugs at ART canter.... 6. Others

33. Alcohol use in past month:

1. Never. 2. Once a month. 3. 2-3 times a month. 4. once/twice a week.

5. 2-3 times a week. 6. Nearly every day.

34. Illigal drugs use? Never..... Past use Daily Occasional

If yes, then have you taken illegal drugs during last six month? Yes No

36. Have you ever injected drugs? yes no

37. If yes, do you currently inject drugs? yes no

VI. Prescription of the treatment

38. Are you satisfied with your treatment? 1=Yes 2=No

39. If No Why?

Data from the medical register

40. CD4 cell count (Cells/mm3)

41. Type of antiretroviral medication

Thank you for taking the time to complete the questionnaire and support this research.

Appendix 2: Letter from Department of Community Medicine



Date: 10 January 2012

To whom it may concern

I hereby confirm that Rajesh Shigdel, born 24.6.1986, is a master student at the University of Tromsø, Norway. The protocol for his Master Thesis project, titled

“Factors associated with Adherence to Antiretroviral Therapy in HIV-infected Patients : A cross-sectional study in Kathmandu Valley”

has been approved by me, as his main supervisor.

He is advised to apply for ethical approval of his study in Nepal

Sincerely,



Elise Klouman
MD, PhD, Associate Professor
Department of Community Medicine
University of Tromsø
Norway

Appendix 3: Ethical approval Letter from Nepal Health Research Council



Nepal Health Research Council

Estd. 1991

NHRC

Ref. No. 1039

Executive Committee

Executive Chairman

Prof. Dr. Chop Lal Bhusal

Vice - Chairman

Dr. Rishi Ram Koirala

Member-Secretary

Dr. Shanker Pratap Singh

Members

Prof. Dr. Meeta Singh

Prof. Dr. Suman Rijal

Dr. Narendra Kumar Singh

Dr. Samjhana Dhakal

Dr. Devi Gurung

Representative

Ministry of Finance

National Planning Commission

Ministry of Health & Population

Chief, Research Committee, IOM

Chairman, Nepal Medical Council

3 April 2012

Mr. Rajesh Shigdel

Principal Investigator

University of Tromso, Norway

Ref: Approval of Research Proposal entitled **Factor associated with adherence to antiretroviral medication in HIV-infected patients :A cross-sectional study in Kathmandu District**

Dear Mr. Shigdel,

It is my pleasure to inform you that the above-mentioned proposal submitted on 2 February 2012 (Reg. no. 14/2012 please use this Reg. No. during further correspondence) has been approved by NHRC Ethical Review Board on 2 April 2012 (2068-12-20).

As per NHRC rules and regulations, the investigator has to strictly follow the protocol stipulated in the proposal. Any change in objective(s), problem statement, research question or hypothesis, methodology, implementation procedure, data management and budget that may be necessary in course of the implementation of the research proposal can only be made so and implemented after prior approval from this council. Thus, it is compulsory to submit the detail of such changes intended or desired with justification prior to actual change in the protocol.

If the researcher requires transfer of the bio samples to other countries, the investigator should apply to the NHRC for the permission.

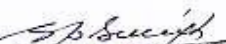
Further, the researchers are directed to strictly abide by the National Ethical Guidelines published by NHRC during the implementation of their research proposal and submit progress report and full or summary report upon completion.

As per your research proposal, total research amount is NRs. 282,000.00 and NHRC processing fee is US\$ 100.00.

If you have any questions, please contact the research section of NHRC

Thanking you.

Sincerely Yours,


Dr. Shanker Pratap Singh
Member Secretary

Appendix 4: Permission Letter for Field work (NCASC)



नेपाल सरकार
स्वास्थ्य तथा जनसंख्या मन्त्रालय

४२६१६५३
४२६२७५३
४२६८२१२

राष्ट्रिय एड्स तथा यौन रोग नियन्त्रण केन्द्र

फ्याक्स: ४२६१६०६

पत्र संख्या:- ०६८-१९९
चलानी नं:- ३२९



ईमेल : ncasc@mos.com.np
वेबसाइट : www.ncasc.gov.np
टेकु, काठमाडौं, नेपाल

मिति : २०६८/१२/१२

विषय :- सहयोग सम्बन्धमा ।

श्री शुकुराज ट्रिफिकल तथा सर्वा रोग अस्पताल, टेकु / शिप्रम अस्पताल, महायजगंज / बीर अस्पताल, काठमाडौं / प्रशुती गृह, बापाथली / माईती नेपाल, गौशाला / स्वर्ग नेपाल, सानेपा ।

प्रस्तुत विषयमा श्री राजेश भिन्देलले निजको Tuberculosis को लागि ART औषधी सेवन गरि रहेका HIV रोगीहरूसँग ART नियमितता सम्बन्धी सूचनाहरूको आवश्यकता भएकोले काठमाडौं भित्रका ART Center हरूमा सूचना संकलनमा सहयोग गरि दिनु हुन भनी यस केन्द्रमा रिपोर्ट दिनु भएकोले, निजलाई सो सम्बन्धमा आवश्यक सहयोग गरि दिनु हुन अनुरोध गर्दछु ।

डा रमेश कुमार श्रेष्ठ
निर्देशक

बोधार्थ :-

श्री राजेश भिन्देल :- अध्ययन पूरा भए पछि १ प्रति प्रतिवेदन यस केन्द्रमा बुझाउनु हुन ।

एड्स रोक्ने प्रतिबद्धता पूरा गरौं ।

Appendix 5: Permission Letter for Fieldwork (TU Teaching Hospital)



TRIBHUVAN UNIVERSITY
TEACHING HOSPITAL

Cable: TUTHMED, KATH

Maharajgunj
Kathmandu, Nepal.

Ref. No.

Date:

२०६८।१।२१

जो जस्ताई सम्बन्धछ ।

उपरोक्त विषयमा राष्ट्रिय एड्स तथा यौन रोग नियन्त्रण केन्द्रको च. न.३२९ प. स. ०६८/६९ को पत्र अनुसार श्री राजेश सिग्देललाई यस अस्पतालमा ART सेवत गरिरहेका HIV संक्रमित व्यक्तिहरूसंग ART नियमितता संबन्धि सूचना संकलन गर्न अनुमति प्रदान गरिएको थियो ।

(प्रा.डा. प्रेम खडगा)

उप संयोजक

एच.आई.भी. एड्स समिति

Appendix 6: Permission Letter for Fieldwork (Bir Hospital)



नेपाल सरकार
स्वास्थ्य तथा जनसंख्या मन्त्रालय
चिकित्सा विज्ञान राष्ट्रिय प्रतिष्ठान
वीर अस्पताल
वीर अस्पताल, महाबौद्ध, काठमाडौं

पत्र संख्या: ०१८-०१९

चलानी नम्बर:- २१२०

महाबौद्ध, काठमाडौं

मिति:- २०६८।१०।१०

विषय :-

अनुमति सम्बन्धमा ।

श्री राजेश सिग्देल
University of Tromso, Norway.

प्रस्तुत विषयमा राष्ट्रिय एड्स तथा यौन रोग नियन्त्रण केन्द्रको प.सं. ०६८।६९, च.नं. ३२९, मिति २०६८।९।१२ को पत्रानुसार तपाईंलाई यस अस्पतालको ART Clinic बाट HIV संक्रमित व्यक्तिहरूसंग ART नियमितता सम्बन्धी सूचना तथा तथ्याङ्क संकलन गर्न अनुमति दिइएको व्यहोरा जानकारी गराईन्छ ।


(प्रा.डा. बुलन्द थापा)

निर्देशक
निर्देशक

बोधार्थ:

डा. शुशिल कुमार शाक्य
ART Clinic, वीर अस्पताल ।

Appendix 7: Permission Letter for Fieldwork (STIDH)

**Government of Nepal**
Ministry of Health & Population
Department of Health Services
Sukraraj Tropical & Infectious Disease Hospital
Teku, Kathmandu, Nepal

Tel. { 4253395
4253396

Ref. _____

Date: _____

March 14, 2012

To
University of Tromso
Tromso, Norway

Re: Permission of information collection

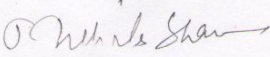
Dear Sir/ Madam,

In reference to the letter of National Centre for AIDS and STD Control (NCASC), ref no-329, letter no-2012, Mr. Rajesh Shigdel has been provided permission dated from 22nd of January 2012 for his research work during his MPH study, to collect information through PLHIV client attending in collaborative ART centre of this Hospital.

The ART centre is established in February 2004 which is one of the largest centres in Nepal. In 2009, an international NGO, AIDS Healthcare Foundation (AHF Nepal) joined to support the ART centre thus it has been functionally called as collaborative ART centre.

I wish all the best in his academic excellence.

Sincerely,


Dr. Mithila Sharma
Director

CC: Rajesh Shigdel, MPH student, University of Tromso