

Determinants of None-adherence to antiretroviral therapy among HIV-infected adults in Arba Minch General Hospital, Gamo Gofa Zone, Southern Ethiopia: A case control study

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Abstract: Background: Non-adherence to antiretroviral therapy is a major challenge to Acquired Immunodeficiency Syndrome (AIDS) care. For Antiretroviral Therapy (ART) to be effective, high level of adherence is required. In spite of this, there is no information on determinant none-adherence to antiretroviral therapy in the study area; therefore this study was conducted to identify predictors of none-adherence to antiretroviral therapy among People Living with HIV/AIDS (PLWHA) in Arba Minch General Hospital. Methods: Unmatched case-control study design was employed on 115 case and 347 controls. Non-adherence to ART is considered as case and adherence to ART is taken as control. Data was collected by using a structured pre-tested questionnaire and by using data abstraction format from ART registration chart. Binary logistic regression analysis was calculated to assess the presence and degree of association between dependent and independent variables; finally multivariate analysis was conducted to identify independent factors for none adherence. Result: From interviewed respondent majority of respondent 304(65.8%) were females and the rest 158(34.2%) were males. From all respondent 209(45%) were in age group 30-39 years. Factors like rural residence 6.30(3.01-13.15), PLWHA who has no family and community support 1.92(1.05-3.51), mobile phone adjusted odds ratio (AOR) 1.20(1.15-3.44), alcohol drinker 5.88(2.86-12.09), malnutrition 2.83(1.18-6.77) and who consume low dietary diversity 7.18(3.43-15.04) and CD4 Count <250 cells/mm³ 2.18(1.05-4.50) are the major identified significant factors for none adherence to ART treatment in the study area. Conclusion and recommendation: PLWHA, who has no family and community support, rural residence, not utilized mobile phone, alcohol drinker, under nutrition, who consume low dietary diversity and those with low CD4 count are major significant determinant factors for non-adherence to ART treatment. Therefore, the capacity to effectively manage the above critical factor is crucial in the success of antiretroviral therapy.

Keywords: Non-Adherence, Antiretroviral Therapy, Case Control, Southern Ethiopia

1. Background

Non-adherence to antiretroviral treatment is the condition of missing doses completely, not following information given by physician, as well as taking drugs inappropriately whereas adherence to antiretroviral treatment is taking 95% or more of the prescribed doses on time and in the correct way, either with or without food [1, 2]. Significant proportions of HIV-infected patients do not

reach high levels of adherence and this can lead to devastating public health problems. Non-adherence to HIV medication is a major reason for treatment failure [3, 4]. It range from 30% to 40% in the United States of America, Latin America, and Europe and in China; in Botswana 46% of patients were none adherent by self-report doses. The level of none adherence reported in Addis Ababa 18.8% based self-report missing dose. Based on the combined indicator of the dose, time and food adherence

measurement was 27.6 % in Jimma Referral Hospital and 25.8% in Yirgalem Hospital, South Ethiopia [5-7]. There are many identified factors for none adherence among the most commonly identified are socio-economic factors and social support, drug abuse and alcohol consumption, ART medication side effect and clinical condition of patient (CD4 count, WHO staging ,opportunistic infection), nutritional related factors under nutrition, dietary diversity and feeding frequency [1, 8]. As a report of Arab Minch Hospital data base shows, there is 10% average non-adherence flow in monthly follow up. As explained above determinant factors are not explored in the study area. Therefore this study aimed to identify factors affecting adherence ART treatment in Arba Minch General Hospital.

2. Methods and Materials

2.1. Study Area, Period and Design

The study was conducted in Arba Minch General Hospital. It is public Hospital located in Gamo Gofa Zone; Southern part of Ethiopia 505 Km away from Addis Ababa and 275 Km away from Hawassa. It provides general Health care service and higher levels of clinical care for catchment area populations. It has been providing highly active antiretroviral therapy (HAART) for PLWHA Starting from 1996 for retroviral infected adults and pediatric Patients. The study employed unmatched case control study design on adults' clients under ART clinics from December 5 /2013 up to February 10/2014.

2.2. Source and Study Population

The study participants were HIV/AIDS positive subjects greater than 18 years who were on ART follow up in Arab Minch General Hospital during data collection period. Pregnant mothers, patient who enrolled on ART less than 3 months ,missing clinical record, incomplete data and those less than 18 years were exclude from the study.

2.3. Sample Size Determination

The sample size was computed by Epi-info version 7 by considering the following assumption a ratio of non-adherent cases to adherent controls of 1:3, power 80, 95% confidence interval (CI), and odd ratio=2. By considering factors that have association with none adherence from recent study conducted in North Ethiopia and Southern Ethiopia in Yirgalem Hospital [1, 9].

$$n_1 = \frac{\left[\frac{Z_{\alpha}}{2} \sqrt{\left(1 + \frac{1}{r}\right) P(1-P)} + Z_{\beta} \sqrt{P_1(1-P_1) + \frac{P_2(1-P_2)}{r}} \right]^2}{(P_1 - P_2)^2}$$

$$r = \frac{n_2}{n_1} \quad P = \frac{P_1 + rP_2}{1+r}$$

n1= number of cases=117, n2= number of controls=350
r= the ratio of cases to controls=1:3(1 None adherence

with 3 Adherence).

P1= proportion of controls among exposed, P2= proportion of cases with exposure

2.4. Sampling Procedure

Study participant was selected based on daily follow up of patient in ART clinic. First non-adherence case was identified from ART by reviewing patient registration follow up charts. Patients were selected; who were non-adherent (poor adherence) at least once in the last three visits follow up appointment. In addition to PLWHA who came for ART follow up by missing monthly follow up screening for non-adherence based on self-report missing prescribed dose less than 95% of the total numbers of the prescribed antiretroviral medication for the last one month were considered as "cases".

2.5. Data Collection Procedure and Tools

Interview administered Amharic version questionnaires was used to collect data on socio demographic and others factors related to none adherence; the questionnaire was adapted and modified in to our context from previous literatures [1, 5-8]. Moreover, Human immunodeficiency virus infection (HIV) related clinical information was extracted from ART registration follow up charts by using data abstraction format. Data on dietary diversity and meal frequency was collected by allowing participant freely to recall the number of meal frequency and food Variety consumed within 24 hours with the help of 12 item questions developed for household and individuals dietary diversity scale prepared by FAO and FANTA. Weight of participants was measured by using standard beam balance and the scale was checked at zero before and after each measurement. Participants' weight was measured after removing heavy clothes and was recorded to the nearest 0.1kg. Height of participant was measured by using the standard measuring scale to the nearest 0.01cm. Four unemployed female diploma nurses recruited as data collectors, and two BSc nurse supervised the data collection. Training was given for data collectors and supervisors.

2.6. Data Quality Control

Pre testing of the questionnaire was conducted on 20 clients in Arba Minch town Health Center a week prior to the actual study; and necessary modification is done according to the gap identified. Interview of participants was carried out in private room. Data collection process was strictly followed day to day by the supervisor and principal investigators and the collected data was checked for completeness and consistency every day by supervisors and principal investigators.

2.7. Data Analysis and Handling

Data was coded and entered into epinfo version 6.0 exported to SPSS Version 20 for analysis. Univariate

analysis was conducting to describe the study population in relation to relevant variables. Bivariate analysis undertaken to assess the presence and degree of association between dependent and independent variables; finally factors that shows association in bivariate analysis and which has P-value less than 0.2 entered in to multiple logistic regression model for controlling confounding factors and to identify significant factors. At the end AOR with 95% CI, P-value <0.05 was considered as significant.

Assessment of dietary diversity was analyzed by categorizing in to three levels as ≤ 3 food items as low, 4-6 food items as medium and ≥ 6 food items as higher level and meal frequency was measured as low when the clients eat less than 3 meals and High when they eat ≥ 3 meal frequency per 24 Hours. Nutritional statuses measured by using WHO BMI classification by taking <18.5 kg/m² as under-nutrition, 18.5kg/m²-24.99 kg/m² taken as normal ≥ 25 kg/m² as pre obesity.

2.8. Operational Definition

Adherence to ART (Control): - is defined as taking one's medicine as prescribed and agreed between the patient and provider which is 95% or more adherences to ART. Which means taking doses no more than two hours before or two hours after the time of a doctor's advice to take doses (95% or more adherence = missing ≤ 2 doses of 30 doses or ≤ 3 doses of 60 doses) [1, 4].

Non-adherence to ART (Case): - is the condition of missing doses completely, not following information given by physician, as well as taking drugs inappropriately. Which means taking doses two or more hours before, and/or two or more hours after the time of a Doctor's advice to take doses or missing doses completely (less than 95% adherence = missing >2 doses of 30 doses or >3 doses of 60 doses [1, 4].

Meal frequency – is the number of reported daily eating occasions by PLWA in a household experienced within a

day. This does not include eating occasions experienced outside home. It classified as good when it is 3 and above with additional snack and poor when it is below 3 meals per day based on HIV/AIDS guide line recommendation.

Dietary diversity – is the number of reported different foods and food groups consumed in a household over a 24-hour period. This does not include food group consumed outside home. It is classified as low < 3 food items, medium 4-6 food items and ≥ 6 food items as higher based on FAO recommendation [6].

2.9. Ethical Consideration

Ethical clearance was obtained from Addis Continental Institute of Public Health. Permission letter was obtained from Arab Minch University post graduate public Health coordinating office and Arba Minch General Hospital. Verbal consent was taken from each participant after clearly explaining the purpose of the study. They were informed to withdraw from study at any time and/or to refrain from responding to questions if they were not interest to participate by any reason. Confidentiality of the data file obtained from respondents was kept in secure place by using codes instead of any personal identifiers.

3. Results

From interviewed participated in the present study 347(75.1%) from adherent group and 115(24.9%) were from non-adherent group with response rate of 98.93%. Majority of respondent 304(65.8%) were females and the rest 158(34.2%) were males. From all respondent 209(45%) were in age group 30-39 years. Among the study participants 375(81.17%) were urban and the rest live in rural. Almost half of study participant were daily workers in there occupational statues and 179(38.7) were educated up to primary school and one third of them were not read and write (table 1).

Table 1. Socio-demographic characteristics of the study participants in Southern Region, Gamo Gofa Zone in Arba Minch General Hospital, 2014

Variable	None adherence	Adherence	Total Frequency %
Sex			
Male	52(45.22)	106(30.55)	158(34.2)
Female	63(57.78)	241(69.45)	304(65.8)
Age			
18 - 29 years	37(32.2)	80(23.00)	117(25.33)
30 - 39 years	52(45.22)	157(45.25)	209(45.24)
40 - 49 years	17(14.78)	64(18.44)	81(17.32)
>50 years	9(7.80)	46(13.12)	55(11.90)
Residence			
Rural	40(34.78)	47(13.55)	87(18.83)
Urban	75(65.22)	300(86.45)	375(81.17)
Religion			
Protestant	23(2.00)	92(26.51)	116(24.10)
Orthodox	86(74.78)	246(70.89)	332(71.9)
Muslim	5(23.22)	9(2.60)	14(3.00)
Education			

Variable	None adherence	Adherence	Total Frequency %
Not read and write	51(44.35)	90(25.94)	141(30.50)
Read and write	4(3.48)	17(4.90)	21(4.50)
Primary school	39(31.30)	140(40.35)	179(38.70)
Secondary and above	21(18.26)	100(28.80)	121(26.20)
Occupation			
Daily laborer	73(63.48)	146(40.08)	219(47.40)
Self employed/business	24(20.87)	100(28.82)	124(26.84)
Government employed	18(15.65)	101(31.10)	119(25.76)

The major reasons raised by respondent for missing of prescribed pills are forget the time, away from home and busy with other work are major reasons raised by respondent (fig 1).

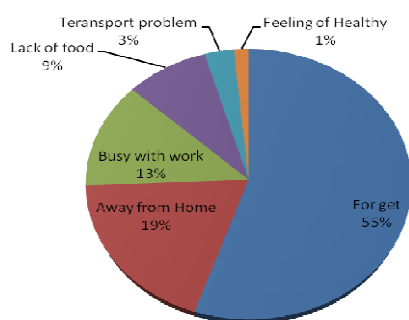


Fig 1. Justification given by respondents for missing prescribed pills In Arba Minch General Hospital, 2014.

3.1. Factors Affecting Non-Adherent to ART Treatment

After applying bivariate and multiple logistic regressions; factors like rural residence 6.30(3.01-13.15), PLWHA who has no family and community support 1.92(1.05-3.51), those who has no mobile phone AOR 1.20(1.15-3.44)), alcohol drinker 5.88(2.86-12.09), malnutrition 2.83(1.18-6.77)and who consume low dietary diversity 7.18(3.43-15.04) and CD4 count <250 cells/mm3 2.18(1.05-4.50) are the major identified significant factors for non-adherence to ART treatment in the study area (table 2).

Table 2. Bivariate and multivariate analysis between explanatory variables and none adherence to ART among study participants in Arba Minch General Hospital, 2014

Explanatory Variable	Adherence statuses		Crude OR (95% CI)	Adjusted OR (95% CI)	AOR P-value
	Non adherent (1)	Adherence (0)			
Sex					
Male	52(45.2)	106(30.5)	1.88(1.23-2.89)	1.35(0.69-2.63)	0.39
Female	63(54.8)	241(69.5)	1	1	
Residence					
Rural	40(34.8)	47(13.5)	3.40(2.08-5.56)	**6.30(3.01-13.15)	0.001
Urban	75(62.2)	300(86.5)	1	1	
Education level					
Not read and write	51(44.3)	90(25.9)	2.69(1.50-4.83)	1.14(0.46-2.86)	0.77
Read and write	4(3.5)	17(4.9)	1.12(0.34-3.67)	0.69(0.15-3.18)	
Primary school	39(33.9)	140(40.3)	1.32(0.74-2.39)	1.47(0.66-3.25)	0.34
Secondary and above	21(18.3)	100(28.9)	1	1	
Occupational statuses					
Daily laborer	73(33.9)	146(42)	2.80(1.58-4.98)	1.73(0.84-3.57)	0.14
Self employed/business	24(20.9)	100(28.8)	1.34(0.68-2.63)	0.751(0.33-1.70)	
Government employed	18(45.2)	101(28.2)	1	1	
Media exposure					
Yes	39(33.9)	186(53.6)	1	1	0.31
No	76(66.1)	161(40.4)	2.25(1.45-3.49)	0.69(0.34-1.42)	
Working Hours					
≤8 Hours	74(63.3)	153(44.0)	1	1	0.68
>8 Hours	41(36.7)	194(56.0)	2.30(1.47-3.54)	1.12(0.96-2.78)	
Mobile phone					
Yes	41(35.6)	213(61.4)	1	1	0.014
No	74(64.4)	134(38.6)	2.85(1.85-4.44)	**1.20(1.15-3.44)	
Getting community /Family support					
Yes	77(66.9)	292(84.2)	1	1	0.035
No	38(33.1)	55(15.8)	2.62(1.61-4.25)	**1.92(1.05-3.51)	

** Significant factors in multiple logistic regressions

Table 2. Continued ...

Explanatory Variable	Adherence statuses		Crude OR COR(95% CI)	Adjusted OR AOR (95% CI)	P-value
	Non-adherent (1)	Adherent (0)			
Side effect of drugs					
Yes	53(46)	100(28.8)	2.11(1.37-3.26)	1.19(0.64-2.26)	0.58
No	62(54)	247(71.2)	1		
Alcohol drinking					
Yes	28(24.3)	27(7.8)	3.81(2.14-6.80)	**5.88(2.86-12.09)	0.001
No	87(75.7)	320(92.2)	1		
Meal frequency					
≤ 2 meals	23(20)	45(12.9)	2.19(1.18-4.03)	0.94(0.49-1.79)	0.032
3 Meals	53(46)	135(38.9)	1.68(1.05-2.69)		
3 Meals with sank	39(24)	167(48.2)	1		
Nutritional statuses(BMI)					
≤18.5	27 (14.8)	53(15.3)	2.29(1.12-4.680)	**2.83(1.18-6.77)	0.01
18.6-24.99	72(62.6)	222(63.9)	1.46(0.79-2.66)		
≥25	16(22.6)	72(20.8)	1	1	
Dietary diversity					
≤ 3 food groups	38(33)	34(9.8)	8.85(4.75-16.49)	**7.18(3.43-15.04)	0.001
4-5 food groups	52(45.2)	115(33.1)	3.58(2.10-6.08)		
≥6 food groups	25(21.2)	198(57.1)	1	1	
WHO stage					
Stage I	68(59.1)	271(78)	1	1	1
Stage II	29(25.2)	49(14.1)	2.36(1.39-4.01)	0.18(0.02-1.36)	0.09
Stage III	13(11.3)	25(7.2)	2.07(1.01-4.26)	0.24(0.03-1.90)	0.17
Stage IV	5(4.4)	2(0.7)	2.35(1.38-4.01)	0.14(0.02-1.27)	0.08
Recent Opportunistic infection					
Yes	50(43.5)	114(32.9)	1.57(1.02-2.42)	1.00(0.51-1.95)	1.00
No	65(56.50)	233(67.1)	1		
Recent CD4 Count					
≤250	25(21.7)	42(12.1)	2.19(1.19-4.00)	**2.18(1.05-4.50)	0.04
251-500	49(42.6)	154(44.4)	1.17(0.73-1.88)		
≥501	41(35.7)	151(43.5)	1		

** Significant factors in multiple logistic regressions

4. Discussion

This study focused on determinant factors affecting none adherence to ART among adult people living with HIV who take antiretroviral therapy. From socio demography factors those who are rural are more likely none adhere than their counter part, these finding is supported by other similar studies [8, 9]. But from occupational status, those daily workers do not show significant association; this finding is consistent with study conducted in Eastern Tanzania and North Ethiopia [1, 2].

Patients who had no family and social support were 1.92(1.05-3.51) times more likely to be none adhere to ART as compared to those who get materials ,financial and advice from their family, religious and social organization; this finding is similar and consistent with other findings [10-12].Social support enhance adherence through encouragement, reassurance, reinforcement, and motivation of to take their drugs properly and regularly by masking the effect of stigma, stress, anxiety and depression [2].

Participant who has no mobile phone 1.20(1.15-3.44)) times more likely to be none adhere to ART as compared to their counterpart. This finding is consistent with other studies [7, 12, 13]. Mobile phone alarms serve as reminders for the patient helps to remember medication time easily

[13, 14]; in addition mobile phone is essential tool for adherence supporters to call patients when they miss their monthly appointment.

Alcohol consumers are 5.88(2.86-12.09) times more likely none adhere to ART as compared to none drinker. These finding is consistent with study done in Eastern Tanzania, Botswana, Cameroon, Northern Ethiopia [1, 2, 4, 15]. Drug abuse and alcohol consumption further threaten proper adherence; active alcohol or substance abuse makes it more difficult for patients to adhere to treatment. Alcohol use can result into forgetfulness of the dose timing and dietary instructions that accompany some antiretroviral medications [2]. Excessive alcohol use can cause liver damage, increase liver enzymes which lead to short drug's half-life than expected. Besides, alcohol exacerbates antiretroviral drug side effects.

Among nutritional related factors; malnutrition (which is defined as BMI<18.5 Kg/m²) was significantly associated with non-adherence to ART. This result is similar and supported by a study conducted in Zambia, Uganda, Northern and Southern Ethiopia [1, 16-18]. Better nutritional status could enhance adherence to ART[1, 19].People living with HIV infection exposed to impaired productivity and declining income these condition enforce them to feed low diet quality and quantity food ;finally

result malnutrition along with HIV infection [17, 20, 21].

Respondent who feed low dietary diversity of food in the last 24 hours were more likely non-adhere to ART than their counterpart. The result is supported by the study done in Peru, Uganda [21, 22]; respondent who did not afford balanced meals. Feeding diversified food improve quality and nutritional content of foods and furthers enhance nutritional statues of patients result for better adherence to ART [1, 17, 19, 20].

Among Clinical, Medication and drug side effect factors CD4 count less than 250 cells/mm³ more likely none adhere to ART as compared to their counterpart; the finding is consistent with another study[1]. From all non-adherence cases in the current study 74(64.3%) of them have CD4 count less than 500 cells/mm³.

In this study opportunistic infection, WHO stage and drugs side effect did not show significant association to none adherence in multivariate analysis these finding is contradicted with others studies [5, 9, 12, 19, 23-25]. In addition majority of the patient take ART medication for long time; they tolerate and adapted drug side effects along with Health professional advice about the side effect of drugs.

5. Conclusion

PLWHA who has no family and community support, who live in rural area, not utilized mobile phone , alcohol drinker, malnourished, who consume low dietary diversity and with low CD4 counts are the major significant factors for None adherence to ART treatment.

6. Strength and Limitation of the Study

Has better strength to identify multiple and Varsity of factors for none adherence to ART treatment specifically socio demography, Nutritional related factors and HIV clinical factors. In addition the data was collected by using different tools like structured interviewed questioners, by direct measuring the Height and Wight by using standard measuring scale and by using data abstraction format this increase internal validity.

The limitation of this study was; it does not include institutional and Health profession related effect on none adherence. It may be affected in some extent by social desirable and recall bias; even it was minimized by different strategy like interviewing in private rooms, by probing to recall freely the frequency and variety food consumed in 24 hours.

Recommendation

For Health Professional

- The adherence supporters should give technical support for PLWHA to take drugs on work place.
- Health professional and Adherence supporters

should adjust and give direction; for RVI patient to have cost effective multiple reminder methods.

For Government and NGOS

- Focus on developing and well integration of alternative income generating activities and social supports to ART programs for PLWHA to improve their nutritional statues and dietary quality based on local context; instead of distributing food supplementation; to improve adherence and to reduce burden of HIV/ADIS on community.

For Researchers

- Further study should be carried out in longitudinal base by integrating with qualitative study design to understand deeply socio-cultural and behavioral related factors towards None adherence because ART adherence is dynamic and its factors are modifiable from time to time.

Abbreviations

ART-Anti Retroviral Therapy, ARV-Antiretroviral, HAART-Highly Active Anti Retroviral Therapy, PLWHA-People living with HIV/AIDS, BMI-Body mass index

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Competing interest

The authors declare that they have no competing interest.

Authors' Contributions

BD: Initiated the research, wrote the research proposal, conducted the research, did data entry and analysis and wrote the manuscript. YB: contributed in the designing of methods and data analysis. EA: contributed in the designing of methods, data analysis and write up of proposal. DM: Involved in designing in Methodology and data analysis.

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