

Evaluation of Adherence Stability to Antiretroviral Therapy in Patients with HIV in Health Care Centers of Tehran In 2014

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Abstract:

Goal: Adherence to antiretroviral therapy (ARVs) in patients with HIV can suppress the virus and stop their replication. When the adherence to treatment is less than desirable, viremia protests will happen and cause increased resistant viral strains, then this lead to failure of treatment. Due to the role and the importance of antiretroviral therapy, adherence stability to antiretroviral therapy in health care centers of Tehran is studied in this research.

Method: This research was done as an observational method and a follow up study in 2014. The information was gathered from 320 patients with HIV over 18 who went to health care centers of Tehran and used antiretroviral therapy at least for 6 months. In order to gather information Beck depression inventory (BDI-II), Beck anxiety inventory (BAI) and demographic variables inventory were used. Descriptive statistical methods (frequency, mean, and percent) and inferential methods such as Long Rank test and proportional hazard ratio model Cox with SPSS and STATA to gain independent prognostic factors with 95% confidence level were used to analyze data.

Results: The results of this research don't show remarkable difference between the mean of non-adherence to treatment and variables like sex, age, job, distance, location, education, pregnancy, menstrual, marital status, stages of the disease, divorce, smoking, drinking, type of treatment regimen, side effects of medications, biological markers (CD4, viral load), while there is a remarkable difference between mean of non-adherence to treatment and variables like addiction, depression, amnesia, anxiety (p-value=.004<0.5).

Conclusion: According to the results of the research and the fact that variables like addiction, depression, amnesia and anxiety have impact on patients, who use antiretroviral treatment, health planning can be held in management level to prevent and control the progression of HIV disease. Doing a Meta analyze study or planning and implementing multinational research to study the impact of these variables seem to be necessary.

Keywords: Adherence stability to treatment, Observational study, Antiretroviral treatment, HIV treatment.

I. Introduction

Increasing HIV disease and infection is a big health challenge of our world. According to WHO in 2011, there are 34 million people with HIV infection in the world that 3/3 million of them are young children under 15. This makes HIV a real challenge. Also the human immunodeficiency virus (HIV) is a real threat to human health in the world. HIV Prevalence is increasing. Implementation of treatment planning even when they are less than desirable, make huge reductions in rates of death (1). Antiretroviral treatment is the basic treatment of HIV. This treatment can not kill or cure the virus however it prevents the growth of the virus in patient's body (4). Treatment consists of drugs which should be taken daily to the end of the life. In addition to improving life quality and longer life, the treatment lead to the reduction of stigma and HIV discrimination among patients (5). The lower the stigma the easier the treatment so that there will be epidemic control and more adherence to treatment among patients (6). Revealing the patient's condition to his spouse or family will be of great help for a patient's who has been infected with HIV. It is essential for patients to have favorable health care available. One of the evaluation methods of ART treatment is the evaluation of adherence rates to antiretroviral therapy in patients with HIV.

This adherence evaluation is done directly or indirectly. In direct method blood concentration, urine and blood metabolites and drug level measurement are determined that is so expensive. Indirect method consists of patient own explanation and information, the amount of taken drugs, missed doses of medication, the evaluation of clinical response electronically which has its own problems (7,8).

Most of studies define desirable adherence as 95% or more consumption of medication (9). There are some factors such as health quality, multidrug, cognitive performance, education, social protection, social environment and suitable transportation which may influence the adherence to treatment (10). Adherence from

social viewpoint shows that social environment in interacting with individuals is quite important; also the way they provide services or care about the patient can be a main obstacle because most of the time they don't offer medication easily (11). Adherence to ARV treatment in Patients with HIV in a place with limited resources remains a concern. All antiretroviral treatment complexities, side effects, intoxication produced by combination of drugs are adherence problems (12). Results show that addicts who have been infected with HIV have less adherence than the other patients (13,14).

Adherence to treatment varies over time. It is not fixed. It's a dynamic process which should be protected completely in all clinical follow-ups (15). Some of the studies in the first or second evaluation from 73.9 to 80.5% report 95% or more adherence to treatment. Also studies report 26/1 and 19/5% as less adherence than 95% in the first and second evaluations (16). In a prospective study on women in 2002, the mean of adherence from 64% in the first month reduced to 45% in the sixth month, about ¼ of participants had 10% adherence reduction during consecutive months (17). In other studies about adherence to ART treatment, based on under studied drugs, the mean of adherence increases from 37% to 83% (18). Moderate proportion of covered doses and combination therapy among urban patients increased from 72% to 79% among rural patients during the first year of treatment. Also aging, white race, lack of alcohol and drug consumption and lack of hepatitis have direct relation with the increase of adherence to treatment (19). In studies a strong relation was reported between treatment regimen and adherence rates, as well drug toxicity, side effects and amnesia have a prominent role adherence reduction to treatment (20).

The relation between depression and adherence was studied in many researches that the more depression the less adherence (21). Among demographic factors in different studies, aging is related to increase of adherence and less age is related to reduction of adherence (16,19). The level of adherence is less among women (25,26). The increase of adherence has been observed among married patients. Denial of treatment, awareness rates and knowledge about HIV, clinical stages of the disease, depression symptoms and being male are considered as important factors in the adherence to ART treatment (24,25). The increase of awareness about treatment and the suitable relation between health care providers and patients lead to favorable results in treatment (26,27). Before starting ART treatment, education and consultation help a lot (28). Results showed that a higher proportion of women despite of their less adherence, stay in the ART treatment process (29). This proves the impact of sex in treatment (30,31).

The increase of viral load and the reduction of CD4 lead to the reduction of adherence (17,23,32). The adherence to treatment can be increased by starting treatment with Zidovudine and Tenovofir. Treatment regimen complexities, side effects, the use of drugs, the patient's diet and drug interactions can reduce the adherence rates (33,34). With regard to all these potential challenges, patients' behavior change over time and unexpected reactions can lead to the lack of adherence; so adherence to ART treatment is a big concern. In general the results show that adherence to ART treatment is a social process not an individual one (35).

Adherence to treatment (ARVs) suppresses and prevents the growth of HIV virus. When the adherence to treatment is less than desirable, viremia protests will happen and cause increased resistant viral strains, then this lead to failure of treatment (32,36). Adherence to ARVs treatment is considered as patient's health progress critical behavior (37,38). This means after counting CD4, this behavior is the strongest way to predict patient's condition toward AIDS and death (39,40). However lack of adherence cannot determine the failure or success of ART by itself. Genetic factors in drug metabolism, severe immune suppression, primary drug resistance, recurrent infections are involved too. Another factor is the lack of skill among health care providers (41). Due to the importance of this issue, the evaluation of adherence stability to antiretroviral treatment in patients with HIV in Tehran health care centers is the main concern of this paper.

II. Literature Review

Haji and colleagues (2008) studied the adherence rates to antiretroviral treatment (HAART) and effective factors on patients with HIV. Their study showed drug side effects and patients' amnesia influence the adherence rates (37).

Dousti Irani and colleagues (2010) studied different factors that make the adherence to treatment regimen easier for patients. Their study showed that anxiety has an important effect on patient's motivation and behavior during the treatment (42).

Achappa and colleagues (2013) studied the adherence rates to antiretroviral treatment among people who suffered from HIV. Their study showed that in general financial problems, dementia treatment, lack of family protection, alcohol consumption, depression, social stigma and drug side effects have direct relation with the reduction of adherence (43).

Amberbir and colleagues (2008) in a prospective study in specialized university hospital of Jimma in Ethiopia in ART treatment unit showed that there is a significant relation between depression and adherence rates (15).

Wasti and colleagues (2012) studied effective factors on adherence to ART treatment in Nepal. Their study showed that non-disclosure of HIV (OR=17.99, P = 0.014), (OR= 12.89P<0.001), alcohol consumption, being female (OR=6.91, P=0.001), lack of education (OR=4.58, P=0.015), drug side effects (OR=6.04, P=0.025) and more than an hour distance to get the health care center (OR=2.84, P=0.035) are involved in studying of adherence (44).

Fumaz and colleagues (2009) studied menstrual disorders in women with HIV-1 and the relation of these disorders with adherence to antiretroviral treatment and sexual behavior and depression symptoms among women under 46. Their study showed a significant relation between menstrual disorders and adherence (p=0.02) (45).

Holstad and colleagues (2006) studied the impact of demographic factors and patients' understanding and their characteristics such as mental factors on antiretroviral treatment. Their study showed that lack of alcohol consumption, severity of disease and sex has direct impact on adherence to treatment (23).

III. Methodology

This study is observational and follow-up to determine effective factors on the adherence rates to treatment. Patients over 18 who have been infected with HIV virus that treated for 6 months will be observed in Tehran health care centers according to demographic factors (age, sex, education, job, out come, distance, marital status), sociological factors of divorce, ostracism from family, psychological factors of depression, amnesia and anxiety and biological factors of CD4 and viral load in the next 6 months of treatment.

In this paper, statistical population includes all patients who suffered from HIV and treated at least for 6 months in Tehran health centers in 2014 and stay in antiretroviral treatment process for the next 6 months. The mean of adherence to treatment is evaluated in two intervals.

Cochran formula calculated sample size of 358 cases. Self report has been used in this study. This study has been done based on medical records of patients, face to face interviews, drug consumption ,missed doses in recent days, Beck inventory to evaluate depression and anxiety , information inventory to determine demographic factors and biological factors.

This study measuring tools are questionnaires. Three standard questionnaires were used: Beck depression inventory (BDI-II), Beck anxiety inventory (BAI) and demographic factors measurement inventory.

The Beck Depression Inventory (BDI-II): It contains 21 questions to measure the feedback and symptoms of depressed patients. It has been prepared based on observation, summarization of attitudes and common symptoms among depressed patients. In other words, it has been selected logically. Generally the content of this questionnaire is depression semiotics, but it has more emphasis on cognitive content. The Beck depression inventory is self assessment which will be completed in five to ten minutes. The test has 21 items related to different symptoms. The patients should answer to these 21 items on a four-point scale from 0 to 4. These items refer to sadness, pessimism, feelings of disability and defeat, guilt, sleep disturbance, loss of appetite and self-loathing.

This means that 2items are dedicated to affection, 11 items to cognition, 2 items to apparent behaviors, 5 items to physical symptoms and 1 item to interpersonal semiotics. This scale determines different depression degrees from weak to severe and its points range is from 0 to 63.

The Beck Anxiety Inventory (BAI): this questionnaire is a 21-item scale that its first choice gets 0 point, the second gets 1 point, the third 2 points and the fourth gets 3 points. If your score is 0 to 7, it means you don't have any anxiety. If it is 8 to 15, you have a weak anxiety, 16-25 shows average and 26-63 indicates severe anxiety. After interviewing and using the available information in patients' medical records and controlling patients' medical questionnaires using STATA, the distribution tables and using descriptive statistics such as mean, standard deviation, and median and percentages and chi-square test for qualitative variables and student-t test for quantitative variables were used. In addition, statistical tests, long rank test, survival rates and multivariate analysis and proportional hazard ratio model Cox were used to find independent predictor factors with 95% confidence level.

IV. Results

Demographic information results have been shown in table (1). According to table

(1), based on Log Rank Cox, there is no significant difference between the mean of non-adherence to treatment and demographic factors (age, sex, job, education, marital status) ($0.05 < p$ -value). Comparing the survival rates of non-adherence to treatment based on Wilcoxon test with (p -value > 0.05), there is no significant difference in survival rates of 1, 3 and 6 months according to demographic factors (table 2).

Table1: Data distribution of adherence and non-adherence to treatment based on demographic factors:

	Demographic factors	frequency	Frequency percent	Adherence to treatment	Frequency percent	Non-adherence to	frequency percent	Mean	SD	p. value
Sex	Male	243	76	101	41.6	142	58.4	3.516	0.148	0.086
	Female	77	24	40	51.9	37	48.1	4.087	0.265	
Age	18-25	14	4.3	6	42.9	8	57.1	3.429	0.629	0.267
	25-35	117	36.5	49	41.9	68	58.1	3.440	0.218	
	35-45	128	40	53	41.4	75	58.6	3.548	0.202	
	Over 45	61	19.2	33	54.1	28	45.9	4.339	0.279	
job	unemployed	122	38.12	56	45.9	66	54.1	3.713	0.214	0.616
	Public sector	13	4.06	5	38.5	8	61.5	3.385	0.601	
	Private sector	177	55.32	75	42.4	102	57.6	3.594	0.173	
	Retired	8	2.5	5	62.5	3	37.5	4.500	0.750	
Distance	Less than 1 hour	271	84.68	121	44.6	150	55.4	3.735	0.139	0.511
	More than 1 hour	49	15.32	20	40.8	29	59.2	3.204	0.350	
Location	City	310	96.8	136	43.9	174	56.1	3.656	0.132	0.733
	Village	10	3.2	5	50	5	50	3.600	0.764	
Education	Elementary	54	16.8	23	42.6	31	57.4	3.567	0.329	0.752
	Intermediate	89	27.8	37	41.6	52	58.4	3.550	0.246	
	diploma	122	38.1	54	44.3	68	55.7	3.583	0.210	
	Above diploma	55	17.3	27	49.1	28	50.9	4.073	0.295	
Income	Without income	109	34	51	46.8	58	53.2	3.761	0.222	0.733
	Less than 500000 Toman	89	27.8	32	40	48	60	3.483	0.258	
	500-800	71	22.1	30	42.3	41	57.7	3.596	0.282	
	Over 800	60	16.1	28	46.7	32	53.3	3.752	0.290	
Marital status	Single	130	40.6	53	40.8	77	59.2	3.501	0.203	0.104
	Married	144	45	72	50	72	50	3.932	0.188	
	Widowed	46	14.4	16	34.8	30	65.2	3.224	0.356	
Pregnancy	Yes	3	1	2	66.7	1	33.3	4.333	0.361	0.185
	No	317	99	139	43.8	178	56.2	4.096	0.267	
Menstruation	Yes	13	41.5	7	53.8	6	46.2	4.231	0.617	0.420
	No	307	58.5	134	43.6	173	56.4	3.630	0.132	
Stages of disease	First	129	40.3	54	41.9	75	58.1	3.554	0.206	0.645
	Second	114	43.7	66	47.1	74	52.9	3.861	0.191	
	Third	45	14	19	42.2	26	57.8	3.435	0.353	
	Fourth	6	2	2	33.3	4	66.7	2.667	0.962	

Table 2: Comparing the survival rates of patients' non-adherence to treatment in 6 months based on demographic factors:

demographic factors	significant level
Sex	0.084
Age	0.128
Job	0.723
Distance	0.132
Location	0.922
Education	0.560
Income	0.770
Pregnancy	0.186
Menstrual	0.407
Marital status	0.056
Stages of disease	0.375

Results of the study based on psychological factors have been shown in table 3. Based on Long Rank Cox test, there is no significant difference between the mean of non-adherence to treatment and psychological factors (divorce, smoking, drinking, family rejection, type of HRT, drugs side effects) ($0.05 < p$ -value). But there is a significant difference between the mean of non-adherence to treatment based on addiction, depression, amnesia and anxiety ($0.05 > p$ -value). Also comparing the survival rates of non-adherence to treatment based on Wilcoxon test there is a significant difference in survival rates of 1, 3 and 6 months of addiction, depression, amnesia and anxiety with $0.05 > p$ -value statistically. But there is no significant difference in survival rates of 1, 3 and 6 months of other psychological, behavior and social variables with p -value > 0.05 (Table 4).

Results of the study based on biological markers have been shown in table 5. According to table 5, based on Long Rank Cox test, there is no significant difference between the mean of non-adherence to treatment

and biological markers (CD4, viral load) (p-value>0.05). there is no significant difference in survival rates of 1, 3 and 6 months according to biological markers statistically based on Wilcoxon test (p-value>0.05) (table6).

Results of studying independent prognosticate factors on adherence rates to treatment showed only amnesia, depression, anxiety and addiction with p-value<0.05 have an impact on adherence to treatment based on Wald test with the value of 0.043 and p-value=0.836>0.05, so they are considered as prognosticate factors. But other variables such as sex, age, divorce, location, pregnancy, rejection from family, viral load, stages of disease, distance, CD4+, job, education, income, menstruation, marital status, smoking, drinking, type of HRT and drugs side effects aren't considered as prognosticate factors p-value>0.05 (table7). At last when the prognosticate factors were determined, Cox multivariate model showed that only two factors of amnesia and depression among those four factors impact the adherence rates to treatment (table 8).

Table3: Data distribution of adherence and non-adherence to treatment based on behavioral, psychological and social factors:

	Behavioral, psychological and social factors	frequency	Frequency percent	Adherence to treatment	Frequency percent	Non-adherence to	Frequency percent	Mean	Standard deviation	p. value
Addiction	Yes	15	4.6	6	40	9	60	3.267	0.629	0.001
	No	162	50.6	85	52.5	77	47.5	4.249	0.169	
	Methadone	143	44.8	50	35	93	65	3.021	0.194	
Depression	0-13 (Negative)	93	29	63	67.7	30	32.3	4.909	0.186	0.00
	14-19 (Low)	47	14.6	22	46.8	25	53.2	3.800	0.333	
	20-28 (Average)	77	24	29	37.7	48	62.3	3.622	0.253	
	29-63 (High)	103	32.4	27	26.2	76	73.8	2.486	0.217	
Divorce	No	287	89.6	129	44.9	158	55.1	3.705	0.136	0.259
	Yes	33	10.4	12	36.4	21	63.6	3.216	0.409	
Amnesia	No	126	39.3	96	76.2	30	23.8	5.230	0.141	0.000
	Sometimes	133	41.5	41	30.8	92	69.2	3.176	0.193	
	Often	44	13.7	4	9.1	40	90.9	1.573	0.216	
	Always	17	5.5	0	0	17	100	1.059	0.059	
Anxiety	0-13 (Negative)	210	65.6	107	51	103	49	3.993	0.157	0.003
	14-19 (Low)	57	17.8	18	31.6	39	68.4	2.895	0.306	
	20-28 (Average)	31	9.6	11	35.5	20	64.5	3.554	0.393	
	29-63 (High)	21	7	5	23.8	16	76.2	2.619	0.459	
Smoking	No	118	36.8	60	50.8	58	49.2	3.993	0.203	0.109
	1-5 cigarettes	36	11.2	16	44.4	20	55.6	2.895	0.383	
	More than 5	138	52	55	39.9	83	60.1	3.554	0.197	
Drinking (alcohol)	Yes	15	4.6	4	26.7	511	73.3	2.467	0.557	0.060
	No	305	95.4	137	44.9	168	55.1	3.714	0.132	
Rejection from family	No	263	82.1	117	44.5	146	55.5	3.693	0.143	0.676
	Yes	57	27.9	24	42.1	33	57.9	3.481	0.309	
Type of HRT	3 pills a day	292	91.2	129	44.2	163	55.8	3.660	0.136	0.728
	4 pills a day	25	7.8	10	40	19	60	3.511	0.463	
	5 pills a day	3	1	2	66.7	1	33.3	4.333	1.361	
Drug side effects	No	216	67.5	94	43.5	122	56.5	3.653	0.158	0.806
	Yes	104	32.5	47	45.2	57	54.8	3.658	0.227	

Table 4: Comparing the survival rates of patients' non-adherence to treatment in 6 months based on behavioral and psychological factors:

Significant level	Demographic level
0.003	Addiction
0.016	Depression
0.313	Divorce
0.006	Amnesia
0.008	Anxiety
0.312	Smoking
0.185	Drinking
0.228	Rejection from family
0.603	Type of HRT
0.515	Drugs side effects

Table5: Data distribution of adherence and non-adherence to treatment based on biological markers (viral load and CD4):

	Behavioral, psychological and social factors	Frequency	Frequency percent	Non-adherence to	Frequency percent	adherence to treatment	Frequency percent	Standard deviation	Mean	
Viral load	Fewer than 50 copies	14	4.3	7	50	7	50	4.857	0.402	0.276
	More than 50 copies	36	11.2	12	33.3	24	66.7	3.111	0.384	
	Without viral load	270	84.5	122	45.2	148	54.8	3.666	0.142	
CD4	Fewer than 100	41	12.8	17	41.5	24	58.5	3.389	0.366	0.711
	100-200	67	20.1	29	43.3	38	56.7	3.512	0.291	
	200-300	51	15.1	20	39.2	31	60.8	3.431	0.319	
	More than 300	161	52	75	46.6	66	53.4	3.853	0.180	

Table 6: Comparing the survival rates of patients' non-adherence to treatment in 6 months based on demographic factors:

Significant level	Biological markers
0.312	Viral load
0.583	CD4

Table 7: Comparing Hazard ratio to determine prognosticate factors:

	Wald	p. value	Hazard ratio
Sex	2.097	0.148	1.307
Age	2.817	0.421	1.384
Divorce	0.883	0.347	0.804
Location	0.059	0.808	1.116
Pregnancy	2.394	0.302	0.516
Rejection from family	0.123	0.726	0.935
Amnesia	73.985	0.000	0.112
Viral load	1.810	0.404	0.779
Stages of disease	1.164	0.762	0.785
Distance	0.357	0.550	0.886
Depression	27.931	0.000	0.320
Anxiety	9.448	0.024	0.548
CD4+	0.972	0.808	1.159
Job	1.272	0.736	1.557
Education	0.863	0.834	1.209
Income	0.791	0.852	0.973
Menstruation	0.467	0.494	0.753
Marital status	3.166	0.205	0.868
Addiction	9.362	0.009	0.878
Smoking	3.222	0.200	0.073
Drinking	2.319	0.128	1.609
Type of HRT	0.447	0.800	1.814
Drug side effects	0.043	0.836	1.034

Table8: Cox multivariate model final results:

Variables	Wald test	Significant level(p-value)
Amnesia	58.32	0.000
Depression	11.217	0.011
Anxiety	0.367	0.947
Addiction	0.085	0.958

V. Conclusion

Antiretroviral treatment is the basic treatment of HIV. This treatment can not kill or cure the virus however it prevents the growth of the virus in patient's body. Treatment consists of taking drugs daily till the end of life (4). Retroviral treatment not only increases the quality of life but also decreases the stigma and HIV discrimination. Reduction of stigma helps patients to get help and go to health care centers easily and increases their adherence to treatment (5).

This paper was done to study the stability rates of adherence to treatment among patients with HIV in Tehran health care centers in 1392. In this study 320 patients include 243 male and 77 female were tested using observational study and questionnaires in order to determine the impact of different factors such as sex, age, education, job, out come, marital status, location, divorce, addiction, drinking, smoking, stages of disease, type

of HRT and drug side effects on the adherence to treatment. Researcher made questionnaires and standard Beck depression and anxiety questionnaires (1961) were used to gather data about adherence to treatment.

The results of studying about adherence to retroviral treatment in Tehran health care centers showed that among different variables there is no significant difference in the mean of sex, age, job, distance, location, education, pregnancy, menstruation, marital status, divorce, smoking, drinking, type of HRT and drug side effects (p -value >0.05). But a significant difference was observed in the mean of addiction, depression, amnesia and anxiety statistically (p -value $=0.004<0.05$).

Cox multivariate test results showed that only two factors of depression and amnesia have impact on the non-adherence to retroviral treatment, evaluations showed that amnesia and drug side effects have impact on the adherence to treatment (37). Dousti and colleagues showed that patients' anxiety influence their performance and motivation to be treated. Amberbir and colleagues (2008) showed a remarkable relation between depression and adherence to treatment. Results of Wasti and colleagues (2012) were contrary to the results of this study. They said there is a significant relation between sex, education, distance, drug side effects and drinking and adherence to treatment. Fumaz and colleagues (2009) showed a relation between menstrual disorders and adherence to treatment but we didn't observe such a relation. In Holstad and colleagues study there is a significant relation between drinking, sex and severity of disease and adherence to treatment which is again in contrary to this study's results.

According to the results and the point that one of the main objectives of policy and health authorities in each region is to find risk factors for diseases, so determining of these risk factors by researchers in order to prevent the disease and the transmission of it to others also to reform the variables is a critical work. Health planning in management level can be of great help to prevent the disease. In addition a Meta analysis study and an implementation of multinational study are required.

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