Adherence to antiretroviral therapy among HIV seropositive patients in northern Greece. Major factors of influence

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Abstract

Background: Adherence to HIV antiretroviral therapy (ART) is of great importance for reducing viral load and the eventual treatment of the patients and minimizing infectivity. This study aimed to investigate adherence to ART among people living with HIV in northern Greece and investigate the factors influencing adherence to ART.

Methods: A correlational study was performed on a cohort of 112 seropositive individuals (100 men and 12 women) with a mean age of 37.14 years. The simplified medication adherence questionnaire (SMAQ) was used to assess adherence. In addition, the perceived available support questionnaire (PAS) for social support assessment was utilized to evaluate the perceived social support.

Results: Approximately 60% of patients were found to be nonadherent to ART. Important factors affecting adherence are educational level, social support, and use of substances.

Conclusions: The results show that a significant proportion of the cohort of patients investigated from northern Greece does not show adherence to ART. Several factors were identified to be of significant influence, which should be taken into consideration by the Greek healthcare providers. HIPPOKRATIA 2020, 24(3): 114-119.

Keywords: HIV, AIDS, adherence, antiretroviral therapy, determinants of adherence, social support

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Introduction

HIV infection is a major health issue around the world. Antiretroviral therapy (ART) as a suitable and effective treatment for HIV infection is well documented[1]. Besides the effectiveness of the antiretroviral drugs themselves, the efficacy of ART is significantly affected by adherence to therapy throughout the life of the HIV seropositive patients[2]. A high level of adherence to ART (>95 %) is necessary to achieve and maintain complete and sustained viral depression to prevent disease and to minimize infectivity[3,4]. However, many HIV seropositive patients have failed to achieve or maintain the adequate levels of adherence required to ensure sustained viral suppression, even though current ART regimens are considered easier to conform to than those of the past[5]. Poor adherence can jeopardize the effectiveness of treatment because it reduces the immunological benefit, increases the hazards of hospital admissions, and increases the hazard of longer duration of hospitalization[6].

Adherence is acknowledged as a complex behavior influenced by a wide range of factors that can be categorized into socio-demographic, health-related, patient-related, treatment-related, and interpersonal factors[7,8]. Healthcare providers need information on these factors that significantly affect adherence to ART to prepare and support patients to obtain and maintain good levels of adherence[2]. Adherence to ART, a crucial determinant and success or failure predictor of treatment outcomes, has become a public health issue[9]. Adherence has been shown to be a predictor of drug resistance[2], recovery of CD4+ cell count[10], and survival[11]. In addition, it has been shown that important factors associated with deterioration of adherence are poor social support[12], use of drugs[13] and individual characteristics, such as age[14] and level of education[15].

Although there is considerable information in the literature regarding adherence to HIV ART, there is no available data for Greece. This information is of particular interest due to the recent socio-economic burden experienced by Greek citizens. The purpose of the present study was to investigate in a cohort of HIV patients from northern Greece: i) the proportion of patients who adhere to ART, ii) the characteristics of patients associated with reduced levels of adherence, and iii) the influence of several socio-economic parameters on adherence.

Methods

Study design

In the present study, the fundamental principles of an observational cross-sectional study were implemented, as the aim was to record the level of adherence and to inves-

tigate the relationship of adherence with perceived social support for seropositive individuals. Independent variables were socio-demographic characteristics of patients and perceived social support of seropositive individuals, while adherence to antiretroviral treatment was considered a dependent variable. The survey was conducted from November 2018 to November 2019. The study's research protocol was approved by the Bioethics and Ethics committee of the School of Medicine of Aristotle University of Thessaloniki (decision No 158, date: 21/11/2018).

Study population and sample

One hundred and twelve HIV seropositive individuals, residents in northern Greece, were selected to participate in the study. The sampling method used in the present study was convenience sampling. The HIV seropositive patients who participated were users of the health care services of Special Infections Units in hospitals of Athens, in the Special Infections Unit of the AHEPA University Hospital, and the National Public Health Organization. The selection of individuals was made randomly during their visit to an appointment for counseling information and/or support. Through a consent form, the patients were informed about the type and purpose of the study, as well as about the anonymity and confidentiality of participants. The inclusion criteria of participants in the study were: a) age ≥18 years, b) no prior diagnosis of mental disorder, and c) sufficient knowledge of writing and reading of the Greek language.

Methodology

The simplified medication adherence questionnaire (SMAQ) was utilized to evaluate adherence to ART[16]. The questionnaire consists of six questions with predetermined short answers that patients should answer. Based on individual responses, each patient was classified as either adherent or non-adherent to ART. The SMAQ scale has been

translated and validated in the Greece sample and showed a high reliability and validity[17]. Perceived available support questionnaire (PAS), a scale of the Berlin Social Support Scales[18], was used to evaluate the perceived social support of people with HIV. The scale consists of seven questions, four of which describe perceived emotional, social support, and the remaining three indicate the material support that individuals perceive to be derived from their social environment. The PAS scale has been translated and validated in a Greek sample and showed high reliability and validity[19]. Questionnaires, due to their practicality and flexibility, are able to identify the concerns of patients. Although patient self-report overestimates 20 % the level of adherence, this method still has significant interpretive ability regarding viral load measurements[20]. Self-reported non-adherence is significantly associated with virological failure[21].

Statistical analysis

IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY) was used for the analysis of the data. Indicators such as frequency (n) and relative frequency (%) were used to represent the results of the SMAQ tool to illustrate the degree of adherence to antiretroviral therapy. Both univariate analyses, using the non-parametric chi-square test, and multivariate analysis, using logistic regression analysis, were used to investigate which characteristics predict the adherence to antiretroviral therapy. Also, logistic regression analyses were used to investigate the effect of social support on antiretroviral therapy adherence. The significance level of the research was set at α =0.05. Results are presented as mean ± standard deviation.

Results
Demographics
The demographic characteristics of the 100 (89.3 %) male and 12 (10.7 %) female participants are presented in Table 1. The mean age of the 112 participants was

Table 1: Demographic characteristics of the 112 HIV seropositive individuals who participated in the current study.

		Number of patients	**%**
Gender	Male	100	89.3
	Female	12	10.7
Place of residence	Large urban area	79	70.5
	District town	24	21.4
	Village	9	8.0
Marital status	Single	78	69.6
	Married	9	8.0
	Divorced	14	12.5
	Living together	11	9.8
Education	Primary	3	2.7
	Middle school	5	4.5
	High school	45	40.2
	University	37	33.0
	Master	18	16.1
	Ph.D.	4	3.6
Employment	Yes	73	65.2
	No	39	34.8

37.14 ± 7.7 years with the sample's age ranging from 25 to 63 years. The majority of the sample resided in a large urban area (n = 79, 70.5%) and were single (n =78, 69.6 %). Regarding the participants' educational level, 40.2 % (n =45) were high school graduates and 33 % (n =37) were university graduates. A smaller number were either primary/middle school graduates (n =8, 7.22 %) or Masters/Ph.D. holders (n =22, 19.7 %). Regarding the employment status of patients, 65.2 % (n =73) of them were working at the time of the survey.

Antiretroviral treatment
Analysis of the data showed that 45.5 % (n =51) of patients received regimens of Integrase Inhibitors (IIs) + Nucleoside Reverse Transcriptase Inhibitors (NRTIs), and 30.4 % (n =34) NRTIs + Non-NRTIs (NNRTIs). A smaller proportion of patients received Protease Inhibitors (PIs) + NNRTIs (n =15, 13.4 %), IIs + NNRTIs (n =8, 7.1 %), IIs + PIs (n =3, 2.7 %) and PIs + NTRIs (n =1, 0.9 %). The mean time from diagnosis was 65.45 ± 53.42 months, with a range from eight to 378 months. The majority of the patients had been diagnosed during the preceding ten years (less than 120 months). The average time from ART initiation was 48.63 ± 50.58 months, ranging from six to 372 months. The majority of the sample had commenced treatment during the preceding eight years (less than 96 months). Also, 71.7 % (n =43) of patients had changed their antiretroviral medication once, 16.7 % (n =10) twice and 10 % (n =6) three times.

Use of substance and smoking
Analysis of the responses revealed that 48.2 % (n =54) of patients had used marijuana, 25 % (n =28) cocaine, 14.3 % (n =16) ketamine, and 13.4 % (n =15) amphetamines. With respect to tobacco, 47.3 % (n =53) did not smoke, 19.6 % (n =22) reported smoking up to ten cigarettes daily, and 26.8 % (n =30) ten to 20 cigarettes per day.

Adherence to ART
Analysis of the data from SMAQ for adherence to ART is presented in Table 2. Results indicate that 59.6 % (n =62) of patients had forgotten to take their medication at least once; 14.3 % (n =15) were careless at times about taking their medication; 18.8 % (n =21) did not take their medication over the last weekend; 27.7 % (n =31) of patients reported that they had not taken their medication for three or more days. A patient was categorized as non-compliant should a non-compliance answer was given to any of the questions, and (in quantification terms) should the patient had missed more than two doses in the preceding week or had not taken any medication for more than two days during the preceding three months. The results showed that 58.93 % (n =66) of patients were found to be nonadherent to ART.

Social support
The analysis of the data of the PAS questionnaire, for the evaluation of the Social Support Scales, revealed that the average of the dimension assessing emotional support was 3.11 ± 0.66 [95 % confidence interval (CI): 2.98-3.23] and the mean value of dimension assessing instrumental support was 3.20 ± 0.74 (95 % CI: 3.06-3.34). The mean of the individual score can range from one to four; the higher the score, the higher the level of social support they perceive to be. These results show that participants had from high to very high emotional and instrumental support.

Influence of demographic parameters on adherence to ART
Analysis of the data from the investigation regarding the influence of the demographic parameters on adherence to ART is presented in Table 3. It was revealed that there was a significant dependence of adherence to ART related to the place of residence, $\chi^2(2) =7.561$, p =0.023, and the educational level, $\chi^2(3) =12.131$, p =0.007. The results show that patients residing in a provincial town are more likely to fail to comply with ART. Moreover, results showed that most post-doctoral/Ph.D. patients were adherent to ART compared to primary, middle school, high school, and

Table 2: Descriptive results of the simplified medication adherence questionnaire (SMAQ) tool, employing six questions, for the evaluation of patient adherence to antiretroviral therapy.

		number of patients	%
Have you ever forgotten to take your medicine?	Yes	62	59.6
	No	42	40.4
You are careless at times about taking your medication	Yes	15	14.3
	No	90	85.7
If at some point you feel bad, you stop taking your medication	Yes	3	2.9
	No	102	97.1
Over the last week, how many times have you not taken your medication?	Never	85	75.9
	1-2 times	26	23.2
	3-5 times	1	0.9
	6-10 times	0	0.0
	More than 10 times	0	0.0
Maybe you didn't take any of your medications last weekend	Yes	21	18.8
	No	91	81.3
In the last three months, how many days have you not taken your medication at all?	Up to 2	81	72.3
	3 and over	31	27.7

Table 3: Chi-square test results of the influence of demographic characteristics on adherence to ART

		Adherence				χ^2	p
		No		Yes			
		n	%	n	%		
Gender	Male	60	60.0	40	40.0	0.443	0.506
	Female	6	50.0	6	50.0		
Place of residence	Large urban area	41	51.9	38	48.1		
	District town	20	83.3	4	16.7	7.561	0.023*
	Village	5	55.6	4	44.4		
Marital status	Single	46	59.0	32	41.0		
	Married	7	77.8	2	22.2		
	Divorced	8	57.1	6	42.9	2.165	0.539
	Living together	5	45.5	6	54.5		
Education	Primary	6	75.0	2	25		
	Middle school	28	62.2	17	37.8		
	High school	26	70.3	11	29.7	12.131	0.007*
	University	6	27.3	16	72.7		
Work	Yes	40	54.8	33	45.2	1.480	0.224
	No	26	66.7	13	33.3		

*: significant result, n: number of participants (frequency).

university graduates. Results from the logistic regression analysis revealed a significant effect of educational level, b =0.487, p <0.019 More specifically, those with a higher educational level have a 1.068 (95% CI: 1.309-2.646) higher likelihood of adhering to ART than those with a lower educational background (Table 4).

Influence of the use of narcotic substances on adherence to ART
Analysis of the chi-square independence test data from the investigation of the influence of narcotic substances on ad-

herence to ART are presented in Table 5. It was revealed that there was a negative dependency between adherence to ART and use of marijuana: χ^2 (1) =12.447, p <0.001; cocaine: χ^2 (1) =8.313, p =0.004; ketamine: χ^2 (1) =3.843, p =0.05; all of the above narcotics in general: χ^2 (1) =12.613, p <0.001. The frequency of marijuana use during the preceding 12 months also had a negative dependency effect on adherence to ART: χ^2 (4) =18.656, p <0.001 (Table 5).

The role of social support on adherence to ART
Analysis of the data by the logistic regression analysis

Table 4: Hierarchical logistic regression results with antiretroviral adherence as dependent variable and demographic variables as independent variables.

Factor	B	SE B	p	95% CI for ExpB		
				Lower	Exp(B)	Upper
Education	0.487	0.207	0.019	1.083	1.627	2.444
Constant	-2.163	0.989	0.007		.034	

-2log (likelihood) =145.71; χ^2 (2) =15.968; p <0.05; R^2=0.052 (Cox & Snell); R^2=.070 (Negelkerke)
CI: confidence interval.

Table 5: Chi-square test results for comparison of adherence rates for substance use.

		Adherence				χ^2	p
		No		Yes			
		n	%	n	%		
Marijuana	Yes	41	75.9	13	24.1	12.447	<0.001*
	No	25	43.1	33	56.9		
Cocaine	Yes	23	82.1	5	17.9	8.313	0.004*
	No	43	51.2	41	48.8		
Ketamine	Yes	13	81.3	3	18.8	3.843	0.050*
	No	53	55.2	43	44.8		
None	Yes	22	41.5	31	58.5	12.613	<0.001*
	No	44	74.6	15	25.4		
If you used marijuana with what frequency have you used it?	Not at all	27	42.2	37	57.8		
	1-2 per month	13	72.2	5	27.8		
	1-2 a week	18	85.7	3	14.3	18.656	<0.001*
	3-4 a week	4	80.0	1	20.0		
	Every day	4	100	0	0.0		

*: significant result, n: number of participants (frequency).

from the investigation of the influence of social support on adherence to ART is presented in Table 6. It was revealed that there is a significant effect of actual support, b =1.630, p =0.005, on adherence to ART. In contrast, no significant effect of emotional support on adherence to ART was observed: b =-0.795, p =0.169. More precisely, the augmentation of the instrumental support by one unit resulted in a 5.1 increase (95% CI: 1.634-15.938) in the likelihood of adherence to ART.

Discussion

The challenge for treating HIV patients is adherence to ART[22]. Adherence is the extent to which a patient takes a drug in the manner recommended by the healthcare provider[1] and has been recognized as an essential factor associated with the success of antiretroviral treatment[11]. The results showed that a considerable proportion of participants in the cohort from northern Greece were found to be nonadherent to ART. More specifically, it was observed that approximately six out of ten participants were nonadherent to ART. Individual statements from the SMAQ tool indicated that the most common reason for non-adherence as reported by participants was forgetting to receive ART. The rate of non-adherence is exceptionally high compared to similar studies in the international field, which have shown that the rate of non-adherence in North America is 48 %, in Africa 17 %, in Asia 17 %, in Europe 38 %, and in south America 38 %[7,23,24]. This difference may be attributed to the recent socio-economic burden imposed on the Greek citizens over the last decade. Analysis of the data showed that factors related to adherence to ART were the place of residence, the educational level, the use of narcotic substances, and social support. An important finding of the study was to highlight the relationship between narcotics and adherence to ART. The results showed that the use of marijuana, cocaine, and ketamine, as well as the increase in the frequency of marijuana use, significantly reduced the likelihood of adherence to ART. The influence of narcotics on adherence to ART has been confirmed in several studies[13,25,26]. Research results have shown that increased social (emotional and practical) support is associated with increased adherence to ART. Similar results have been found in studies investigating the role of social support

in enhancing adherence[12,27,28]. Social and psychological variables are among the most important factors affecting adherence to a treatment[27].

In conclusion, this study identified important factors such as place of residence, level of education, use of narcotic substances, and social support that affect short-term adherence for a cohort of HIV patients from northern Greece.

Limitations of the study and future work

The study was conducted using a convenience sample, and the findings may not be generalizable to other clinical settings or a broader range of patients receiving ART. In addition, this study was based on a cross-sectional study design. Therefore, the time relationship between the variables studied is unknown, so that no causal relationship can be established. In addition, cross-sectional research in this study could only measure the level of adherence at one-time point, while medication adherence is dynamic and participants' behavior may change over time. A patient who has been identified today as having complied with ART may not be compliant tomorrow. Care must be taken in interpreting the direction of causality.

The present study results, taking into account the study's limitations, are the first reported for Greece and are in close agreement with those reported in the literature for most other countries. It is necessary to investigate factors related to long-term adherence to ART and its long-term maintenance (e.g., use of reminder tools, telemedicine). The impact of these factors on treatment outcomes may be subject to potential bias. Therefore, it would be useful to evaluate the impact of these factors using randomized controlled trials to obtain more reliable data before applying these findings to clinical practice.

Conflict of interest

Authors declare no conflicts of interest

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Table 6: Results of logistic regression analysis with dependent variable on adherence to antiretroviral treatment and independent variables related to perceived social support.

Factors	B	SE B	p	95% CI for ExpB		
				Lower	Exp(B)	Upper
Emotional support	-0.795	0.578	0.169	0.146	0.452	1.402
Instrumental support	1.630	0.581	0.005	1.634	5.104	15.938
Constant	-3.210	1.144	0.005		0.040	

-2log (likelihood) =136.2; χ^2(2) =13.65; p <0.01; R^2=0.16 (Cox & Snell); R^2=0.156 (Negelkerke)

CI: confidence interval.

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