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The Survival Rate and Its Predictors in HIV-Infected Patients of Kurdistan Province, Iran: A Retrospective Cohort Study

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Research note

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Abstract

Objective: This study aimed to understand the prognostic factors that influence the progress and death in human immunodeficiency virus (HIV) / acquired immunodeficiency syndrome (AIDS) patients in developing countries. This study conducted in the Kurdistan Province, Iran from September 1988 to April 2020. Interest outcomes were time-estimated: (1) from HIV to AIDS and (2) from AIDS to death. The Cox proportional-hazard model also was used in order to consider the effects of different factors on survival rate.

Results: A total number of 591 HIV-infected patients were assessed and the results showed that 1-year, 5-year, and 10-year probability of disease progression from HIV diagnosis to AIDS was 96%, 92%, and 88%, and that of death was 69%, 47%, and 27%, respectively. Cox's multivariate analysis result's showed the following factors were significantly related to AIDS progression: the first CD4 count under 500, using ART, and history of drug use with hazard ratio of 1.93, 4.53, and 0.76, respectively. The mortality was significantly associated with unemployment, using ART with HR of 3.4, and 0.07, respectively. Unemployed AIDS-patients are also more likely to die; this, which need more attention in Iran.

Introduction

The human immunodeficiency virus (HIV) and the acquired immunodeficiency syndrome (AIDS) are still public health challenges throughout the world, especially in developing countries. To our knowledge, there is no definite treatment for AIDS at this time so that can remove the virus from the body. Recently the rate of HIV-related mortality has decreased due to the use of widespread antiretroviral therapy (ART). In fact, with the advent of antiretroviral medications, HIV-infected patients can live longer and have hope for a healthy life after diagnosis [1].

Based on evidence, a number of people living with HIV (PLHIV) have been reduced by 17% over the past ten years in all over the world [2]. In spite of the decrease in HIV/AIDS-related mortality in the recent years, knowledge related to the factors affecting the HIV progression and mortality, and also factors can be related to the increase of life expectancy in PLHIV, especially in developing countries is not sufficient. The leading causes of HIV transmission in patients include unprotected sex (homosexuals, the opposite sex or multiple sexual partners) and sharing injecting drug use [3]. Addiction and in particular injection-addicted is one of the main ways of HIV transition in Iran [4].

According to the previous studies male gender, advanced age, singleness, low educational level, decreased level of CD4 cell count, HIV/Tuberculosis (TB) co-infection, non-compliance with ART and substance drug abuse have been significantly associated with the survival of patients. [5–12]

Designing effective therapeutic approaches to boost the life expectancy of HIV-infected patients needs accurate knowledge about the predictors of HIV/ AIDS progression. Therefore, the aim of this retrospective cohort study was to estimate the time from the HIV diagnosis to AIDS progression and the time from AIDS initiation to the AIDS-related death and also determining their influencing factors.

Materials And Methods

This was a registry-based retrospective cohort study conducted in the Kurdistan Province, Iran from September 1988 to April 2020. The study design was approved by the research council of Kurdistan University of Medical Sciences (IR.MUK.REC.1396/169). HIV positive people who were recorded in five behavioral disease counseling centers in the Kurdistan province, northwest of Iran were included in the study. It should be noted that the mission of this centers is providing several health services including education, pre/post-HIV test counseling, harm reduction and treatment for PLHIV or persons at high risk of HIV and sexually transmitted infection (STI).

To collect the required data, we used a checklist of variables that developed based on the registered medical records of the investigated patients. The checklist contains demographic information (gender, age, job, marital status and level of educations), behavioral information (drug use, drug injecting, and imprisonment), first CD4 count, coinfection with TB and ART use.

According to HIV surveillance program in Iran, an HIV positive case is defined as a person with HIV infection, regardless of clinical stage and confirmed by laboratory criteria based on the country's definitions and requirements. In Iran, a person with two sequential enzyme-linked immunosorbent assay (ELSA) test positive followed antibody's HIV and validated by a western blot test considered as HIV positive. A case of AIDS was specified as a definitive diagnosis of stage 4 conditions or CD4 count less than 350 per mm^2 of blood in an HIV-infected person.

The interesting outcomes were estimated the duration of time of (1) primary outcome: HIV diagnosis to AIDS progression and (2) secondary outcome: AIDS diagnosis to AIDS-related death. The HIV diagnosis to AIDS progression outcome was calculated by subtracting the date of AIDS progression from the date on which the patient was diagnosed with HIV. The other interesting outcome was determined by subtracting the date of AIDS-related death from the date of AIDS progression.

Mean (± SD) and frequencies (%) were used to describe the demographic and clinical characteristics of the study subjects. To estimate the probabilities of progression to AIDS and death the Kaplan-Meier test method was used. Also, to assess the impacts of prognostic factors on the survival rates bivariate (unadjusted) and multivariate (adjusted for all significant variables in bivariate) Cox proportional hazard model was used. Hazard ratio (HR) with a 95% confidence interval (CI) was reported. All statistical analyses were conducted using Stata 14 at a significant level of 0.05.

Results And Discussion

In this study, based on data from the Kurdistan HIV/AIDS surveillance system, from September 1988 to April 2020, there were 597 cases have been diagnosed and registered with HIV. We excluding 6 cases, because they were not Kurdistan dweller. The mean (SD) age of patients was 45.3 (0.4), varied from 4 to 74.

The distribution of the investigated characteristics is shown in Supplementary table 1. From 591 infected-patients 522 (88.3%) of them were not entered to the AIDS stage, 69 (11.9) have been diagnosed with HIV/AIDS, 278 (47%) patients died and 98 (16.6%) patients had been lost to follow up. More than 50% of the patient were aged 45–74, 76% had an education level less than a diploma, 63.6% were unemployed and 50.6% were widows. The majority of the HIV positive patients had a history of drug abuse, drug injection and prison. About half of HIV positive patients had used antiretroviral and just 1.4% of them were co-infected with TB.

Table 1
The Survival time for progression from HIV to AIDS, HIV to death and AIDS to death

Survival time (year)	Total	Event	Censored	Survival probability	SE	95% CI
From HIV to AIDS						
1	557	5	18	0.96	0.007	0.94–0.97
2	534	4	21	0.95	0.008	0.93–0.97
3	509	6	14	0.94	0.009	0.92–0.95
4	489	2	18	0.94	0.009	0.92–0.95
5	469	7	16	0.92	0.011	0.90–0.94
6	446	7	16	0.91	0.012	0.88–0.93
7	423	3	13	0.90	0.01	0.88–0.93
8	407	4	11	0.89	0.01	0.87–0.92
9	392	3	16	0.89	0.01	0.86–0.91
10	373	4	23	0.88	0.01	0.85–0.90
From HIV to Death						
1	501	47	5	0.77	0.01	0.082–0.88
2	454	46	0	0.69	0.02	0.65–0.73
3	408	48	0	0.61	0.02	0.57–0.65
4	360	31	0	0.56	0.02	0.52–0.6
5	329	32	0	0.5	0.02	0.46–0.54
6	297	29	0	0.45	0.02	0.41–0.49
7	268	21	0	0.42	0.02	0..38-0.46
8	247	22	0	0.38	0.02	0.34–0.42
9	225	30	0	0.33	0.01	0.29–0.37
10	195	24	0	0.25	0.01	0.22–0.29
From AIDS to Death						
1	43	1	6	0.69	0.05	0.58–0.8
2	36	0	2	0.69	0.05	0.56–0.78
3	34	3	3	0.62	0.02	0.49–0.7
4	28	3	15	0.53	0.07	0.38–0.66

Survival time (year)	Total	Event	Censored	Survival probability	SE	95% CI
5	10	1	2	0.47	0.08	0.3–0.63
6	7	0	2	0.47	0.08	0.3–0.63
7	5	0	1	0.47	0.08	0.3–0.63
8	4	0	3			

The survival rate for progression from HIV to AIDS, HIV to death and AIDS to death are presented in Table 1. Based on the results, the one-year, 5-year, and 10-year survival rates from HIV to AIDS were 96%, 92%, and 88%, respectively. Moreover, the survival rate from HIV to death in one-year, 5-year, and 10-year were 77%, 50%, and 25%, respectively. From AIDS onset to death, the one-year, and 5-year survival rates were 69% and 47%. Supplementary Fig. 1 is shown the impact of gender and history of drug abuse from the diagnosis of HIV to AIDS, and from AIDS to death.

The effect of the predictors of progression from HIV to AIDS and from AIDS to death is shown in Tables 2 and 3, respectively. According to the multivariate analysis using Cox's proportional hazard model, there was a statistically significant association between duration from HIV diagnosis to AIDS and the first CD4 count under 500, using ART, and history of drug use with the hazard ratio of 1.93, 4.53, and 0.76, respectively. Furthermore, there was a statistically significant association between death resulted from HIV and some investigated factors such as unemployment, using ART with HR of 3.4 and 0.07, respectively.

Table 2
Effect of predictors on survival times from HIV diagnosis to AIDS using the Cox regression

Variable	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Gender				
Female	1			
Male	1.15 (0.4–2.9)	0.7		
Age Group (year)				
0–44	1			
45–74	0.6(0.4–1.01)	0.05		
Education				
Illiterate	1			
Under diploma	2.92(0.7–11.9)	0.1		
Academic	3.11(0.4–22.1)	0.2		
Occupation				
Employed	1			
Unemployed	0.7(0.4–1.2)	0.2		
History of marriage				
No	1			
Yes	1.17(0.6–2.2)	0.6		
Modes of HIV transmission				
Injection drug users	1			
Sexual	1.98(1.06–3.7)	0.03		
Mother to child/Blood	0.99(0.14–7.2)	0.9		
First CD4				
500+	1		1	
0-500	2.01(1.2–3.4)	0.009	1.93(1.1–3.3)	0.01
Antiretroviral therapy				
No	1		1	
Yes	14.4(6.2–33.4)	0.000	4.53(1.6–12.6)	0.004
History of drug use				

Variable	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
No	1		1	
Yes	0.46(0.2–0.8)	0.009	0.76(0.4–1.3)	0.03
History of injection				
No	1			
Yes	0.4(0.09–1.7)	0.2		
History of prison				
No	1			
Yes	0.6(0.3–1.1)	0.1		

The study aimed was to investigate the relationship between demographic, social, epidemiological and clinical features of HIV-infected patients with disease progression and mortality. The results of the multivariate analysis showed that lower CD4 at the beginning of HIV diagnosis, sexual transmission of HIV, drug use, use and non-adherence to ART can shorten the duration between HIV diagnosis and disease progression [2]. The results also indicated that unemployment, sexual transmission and non-adherence to ART can increase the risk of death in HIV/AIDS patients.

Table 3
Effect of predictors on survival times from AIDS diagnosis to Death using the Cox regression

Variable	Unadjusted HR (95% CI)	P-value	Adjusted HP (95% CI)	P-value
Gender				
Female	1			
Male	1.07 (0.25–4.5)	0.9		
Age Group (year)				
0–44	1			
45–74	1.2(0.57–2.6)	0.6		
Education				
Illiterate	1			
Under diploma	0.13(0.02–0.6)	0.01		
Academic	0.25(0.03-2)	0.19		
Occupation				
Employed	1		1	
Unemployed	3.8(1.32–11.11)	0.01	3.4(1.16–9.9)	0.02
History of marriage				
No	1			
Yes	2.15(0.6–7.4)	0.2		
Modes of HIV transmission				
Injection drug users	1			
Sexual	0.47(0.14–1.6)	0.2		
Mother to child/Blood	1.27(0.17–9.5)	0.8		
First CD4				
500+	1			
0-500	1.5(0.6–3.9)	0.3		
Antiretroviral therapy				
No	1		1	
Yes	0.06(0.02–0.2)	0.000	0.07 (0.02–0.22)	0.000
History of drug use				

Variable	Unadjusted HR (95% CI)	P-value	Adjusted HP (95% CI)	P-value
No	1			
Yes	1.67(0.63–4.4)	0.3		
History of injection				
No	1			
Yes	21.6(0.002-Inf+)	0.5		
History of prison				
No	1			
Yes	1.8(0.6–5.4)	0.2		

In our study, the survival rate from HIV to death in one-year, 5-year, and 10-year were 77%, 50%, and 25%, respectively. Liu Z Q et al. in their conducted study on HIV positive patients in China reached the 91%, 86%, and 79% in one- year, five- year and ten- years survival rates, respectively [13]. In Italy, the 10-year survival rate of HIV infected patients in 2012 were 44.7% [14]. It seems that the survival rate of HIV positive patients in developing countries is lower than more developed countries.

Our results indicated that the level of CD4 cells count in the time of HIV diagnosis is an independent predictor of poor survival. This finding is also supported by several previous studies [15, 16]. Lower CD4 cells count can be the main reason for a higher risk of opportunistic complications (infections or malignancies) in patients with HIV/AIDS.

Based on the evidence, until the introduction of Highly Active Antiretroviral Therapy (HAART), age was a strong predictor of HIV progression and death risk [17]. In this study, we did not observe a statistically significant relationship between age group and disease progression or mortality.

The results revealed that poor social situations or unemployment is an independent predictor for mortality in patients with HIV/AIDS. In fact, unemployment is a major problem of HIV infected patients in Iran [18]. This finding is also supported by a study of DeSilva in Jos, Nigeria [19] and Delpierre et al. in France [20].

According to the results, non-adherence to ART is the main risk factor for HIV progression and mortality. The role of ARTs as a therapeutic/preventive effective strategy in the control of HIV/AIDS in many different countries is undeniable [6]. ART improves the immune system, quality of life, life expectancy and is a highly effective protective factor to progression from AIDS to death in AIDS patients [16, 21, 22]. So that promoting ART coverage in countries involving the HIV/AIDS epidemic is one of the most important goals of world health organization. In fact, effective ART is the main intervention to improve longevity and prevent opportunistic infections in patients with HIV/AIDS. This strategy is now a critical component

of HIV prevention in the world [23]. Fortunately, today there are many ART drugs approved for HIV-infected adult patients and are gaining Food and Drug Administration (FDA) approval for use in children.

Another risk factors for HIV progression that found in our study was drug use. Injecting drug use is a barrier to receive ARV [24]. Raposeiras et.al. showed that Tobacco, illicit drugs use and risk of cardiovascular disease in patients living with HIV [25]. The study conducted by Parashar et al. is confirmed by our findings [26]. The results also showed that sexual transmission of HIV is significantly associated with the survival of HIV infected patients. This finding is consistent with other studies that conducted by Maracy et al. in Iran [27].

The main strength of our study was using the registry-based database of all HIV/AIDS patients in the Kurdistan province combined with a long and nearly complete follow-up of patients. Additionally, access to comprehensive Iran death registry database allowed us to specify all deaths which have been occurred for HIV patients because some patients occasionally did not seek routine care, and may have died so that to obtain accurate data, all of the patients who did not seek routine health services were followed up using the national death registry software.

The research findings illustrated that non-adherence to ART is the main risk factors in the incidence of AIDS and HIV-related mortality. Unemployed AIDS-patients are also more likely to die; this, which needs more attention in Iran.

Limitation

Our study has some limitations. In this study, we assessed the effect of some predicting factors for the progression of HIV and may there are several other factors that we did not evaluate. For example, in the previous studies have been shown that TB co-infection and low body max index (BMI) correlated with mortality in HIV infected patients [28, 29], while we could not assess the effect of these main factors in mortality and disease progression of HIV infected persons due to lack of required data. Second, left censoring in our data is undeniable, because we don’t know the date of HIV onset, therefore the date of HIV diagnosis was considered as HIV onset and this issue might lead to underestimation of the actual time of duration from HIV to AIDS stage.

Abbreviations

HIV: Human immunodeficiency virus; AIDS: Immunodeficiency syndrome; ART: Antiretroviral therapy; PLHIV: People living with HIV; STI: Sexually transmitted infection; TB: Tuberculosis; ELSA: Enzyme-linked immunosorbent assay; HR: Hazard ratio; CI: Confidence interval; HAART: Highly active antiretroviral Therapy; FDA: Food and Drug Administration; BMI: Body max index;

Declarations

Ethics approval and consent to participate

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Consent to publish

Not applicable.

Availability of data and materials

The data are available upon reasonable requests from the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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This study has been approved by the Research Council of the University of Medical Sciences of Kurdistan.

Authors' Contributions

The research topic was constructed by SD, KR, OH, the idea was investigated, the statistical analysis was performed and the manuscript was drafted. SD, OH, KR, SS, SK, SH provided the data and participated in the preparation of interpretations and manuscripts. The final manuscript was read and approved by all authors.

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