Survival Rate and Mean Interval between HIV Diagnosis and the Emergence of AIDS Clinical Symptoms in Patients Referring to Behavioral Diseases Health Center of Yazd of Iran from January 2003 to March 2017

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Abstract

Introduction: HIV / AIDS has become a major social problem, and despite the major steps taken to control the disease, it remains as the world's pandemic. In order to achieve the goals outlined in the HIV/AIDS epidemic control, a comprehensive approach that identifies patients with HIV at an early stage is required to integrate patients into a comprehensive and dynamic care system, and provide appropriate and favorable treatment. **Objective:** The present study aimed to determine the survival rate and mean interval between HIV infection diagnosis and emergence of clinical symptoms of AIDS in patients referring to the Behavioral Diseases Center of Yazd Province (Iran) from January 2003 to March 2017. **Materials and Methods:** In this descriptive study, 100 patients who referred to the Behavioral Disease Control Center of Yazd province, January 2003 to March 2017, were studied. Necessary information was collected by the researcher using a checklist containing patients' demographic, clinical, and therapeutic information and their survival status, extracted from the medical records, without recording their names and by maintaining the data confidentiality. Then, descriptive statistics, Chi-Square, T-test, and Kaplan-Meier survival tests were used with a 95% confidence interval (CI) (P-value≤0.05) using SPSS software Ver 23. **Results:** In this study, the mean interval between HIV infection diagnosis and the first disease indicative of AIDS in men was 2958 ± 271 and in women 2476 ± 397 days, which was significantly associated with age (P = 0.003), indigenousness or non-indigenousness (P=0.004) and disease transmission method (P=0.011), but had no significant relationship with gender (P = 0.654) and educational level (P=0.16). Also, this study showed that the mean survival rate of patients after HIV diagnosis was 4338 ± 189 days: 4304 ± 219 days in men and 4187 ± 327 days in women, which was not significantly different (P = 0.805). Mean survival was associated with age (P=0.891), gender (P=0.805), indigenous (P = 0.192), disease transmission method (P=0.214), and education (P=0.466). **Conclusion:** The results of this study and similar studies indicated this obvious principle that it is necessary to minimize the interval between the viral infection and diagnosis of the disease to control the disease, improve the quality of life of patients, and reduce years of potential life lost and we should not delay follow up and treatment of the disease until one of the clinical signs of the disease develops.

Keywords: HIV infection, AIDS, Survival rate

INTRODUCTION

According to the estimations of World Health Organization (WHO), at least 37 million people have become infected with HIV/AIDS around the world by the end of 2016, and nearly 2 million people will be added each year, while only 20 million patients receive antiviral treatment [1]. HIV/AIDS infection has become a major social problem [2], and despite major steps taken to control the disease, it remains pandemic in the world [3]. The United Nations Program on HIV/AIDS (UNAIDS) reported in July 2017 that only 70% of patients with HIV infection are aware of their illness, among whom 77% (19.5 million people) are treated appropriately with antiretroviral drugs and 82% had successful treatment [4]. UNAIDS emphasized in its report that preventing the worldwide spread of the disease is impossible without

starting treatment for people in need [3]. UNAIDS designed a large target for controlling the spread of HIV/AIDS, called "90, 90, 90." Accordingly, by 2020, 90% of patients with HIV infection should be identified, 90% of those identified should receive appropriate antiretroviral treatments, and the virus should be suppressed in 90% of the patients being treated. Realizing this goal will end this epidemic infection and prevent its spread [3]. To achieve this goal, various strategies must be implemented, including broad screening, universal access to treatments with minimal side effects and high efficacy, low costs of care and treatment, and elimination of discrimination related to this infection [5]. HIV treatment is a fundamental principle in reducing the disease transmission, increasing patients' life expectancy, and reducing the complications of this infection [6]. Combined antiretroviral therapy (ART) has changed AIDS from an acute to a chronic disease in countries where treatment is widely used [7]. With current treatments, patients with AIDS can have a lifespan close to life expectancy [8].

To achieve the depicted goals in epidemic control of HIV/AIDS, a comprehensive approach is required, in which patients with HIV should be diagnosed at the beginning of catching the disease and be integrated into a comprehensive and dynamic care system, and receive appropriate and favorable treatment [9]. In this regard, knowing the accurate time of transmission before emergence of clinical symptoms is very important to the community and care system and can indicate the effectiveness of that care system. The present study aimed to determine the survival rate and mean interval between HIV infection diagnosis and emergence of AIDS clinical symptoms in patients referring to the Behavioral Diseases Center of Yazd Province (Iran) from January 2003 to March 2017.

METHOD

In this descriptive study, 100 patients who referred to the Behavioral Disease Control Center of Yazd province January 2003 to March 2017 were studied.

To collect data, a checklist was used that included age, sex, educational level, place of residence (urban or rural, indigenousness or non-indigenousness), the disease transmission method, time of diagnosis of HIV infection, time of the emergence of the first clinical symptom of AIDS. The study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences of Yazd, and the information of all participants in the study was kept confidential without registering patients' names.

The data extracted from checklists were categorized and input into SPSS 23 (IBM SPSS Statistics 23). Data was reported by descriptive indexes such as mean, standard deviation (SD), median and frequency and analyzed by statistical tests, including T Test, Chi-Square, and Kaplan-Meyer survival test. The confidence interval used for significant differences was 95% (P≤0.05).

RESULTS

In this study, 100 patients with AIDS with a mean age of 39±9.97 years were studied. The participants' minimum age was 9 and the maximum was 66 years; 75 cases were male and 25 were female. The mean age of men was 39.61 ± 9.72 years and that of women was 37.61 ± 10.66 years and no statistically significant difference was observed between them (P = 0.289). Other demographic characteristics of patients are shown in Table 1.

Table 1 : Demographic characteristics of participants in the study

Variable		Frequency	Percent
Sex	Female	25	25
	Male	75	75
Age category	<40 years	49	49
	≥40 years old	51	51
Educational level	Illiterate	9	9
	Elementary school	33	33
	Secondary school	32	32
	High school Diploma	17	17
	Academic degree	9	9
Indigenousness	Indigenous	73	73
	Non-Indigenous	27	27
Place of residence	Urban	96	96
	Rural	4	4

A total 65 patients (65%) were infected through contaminated syringe, 28 (28%) through sexual contact, 5 patients (5%) through mother-to-child transmission, and 2 (2%) through other means of transmission. Men were infected through HIV-contaminated syringes (85.3%) more and women were infected through sexual contact (88%) more, which had a significant difference (P≤0.001). Table 2 lists the frequency distribution of HIV transmission methods for both sexes.

Table 2: Frequency distribution of infection transmission method of HIV according to patients' sex

Sex Method of transmission method	Male		Female		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Contaminated syringe	64	85.3	1	4	65	65
Sexual contact	6	8	22	88	28	28

Others	5	6.7	2	8	7	7
Total	75	100	25	100	100	100

Chi-square Test. P ≤ 0.001

In patients indigenous to the study area, infection transmission through contaminated syringe was 65.8% (48 patients), through sexual contact was 26% (19 patients) and through other transmission methods was 8.2% (6 patients) and in non-indigenous patients 63% (17 patients) acquired the disease through contaminated syringe, 33.3% (9 patients) through sexual contact, and 3.7% (1 person) through other transmission methods.

The Kaplan-Meier survival analysis method was used to determine the interval between the time of HIV infection diagnosis and the first diagnosis of AIDS. Based on the results, the mean interval between diagnosis and observation of the first disease was 2913 ± 292 days: 2958 ± 271 days in men and 2476 ± 397 days in women, while no statistically significant difference was observed between them (P = 0.654). Also, the mean interval in patients younger than 40 years of age was 2015 ± 309 (median: 1696 days) and in patients with an age ≥40 years was 303 ± 3570 days (median: 4657 days), which had a significant difference (P = 0.003). The mean time interval in patients with educational level below high school diploma was 3023 ± 256 days (median: 3617 days), and in the patients with an academic degree was 2330 ± 453 days (median: 2726 days), while this difference was not significant (P = 0.156). The interval between HIV infection diagnosis and the first disease indicating AIDS was 3223 ± 247 (3617 days) in indigenous patients and 1847 ± 448 days (519 days) in non-indigenous patients, which showed a significant difference (P = 0.004). This interval was 3199 ± 286 (4657 days) in patients infected with contaminated syringe, 2455 ± 243 (2726 days) in patients with sexual transmission, and 974 ± 505 days (387 days) in the other cases with a significant difference (P = 0.011).

The Kaplan-Meier Survival Analysis method was used to determine the survival rate of patients with HIV infection. Based on the results, the mean survival rate was 4338 ± 189 days after diagnosis of HIV infection: 4304 ± 219 days in men and 4187 ± 327 days in women, which had no statistically significant difference (P = 0.805). Table 3 shows the mean survival of patients according to demographic variables.

Table 3: Mean survival of patients according to demographic variables

Variable		Mean	Standard deviation	P-value
Sex	Female	4187	327	0.805
	Man	4304	219	
Age category	<40 years	4074	261	0.891
	≥ 40 years old	4328	255	
Transmission method	Contaminated syringe	4402	223	0.214
	Sexual contact	4234	307	
	Other methods	2708	866	
Indigenousness	Indigenous	4344	190	0.192
	Non-Indigenous	3912	462	
Educational level	Below diploma	4163	205	0.466
	Academic degress	4628	347	

DISCUSSION

Acquired Immunodeficiency Syndrome (AIDS) in patients infected with Human Immunodeficiency Virus (HIV) impairs the immune system and causes opportunistic infections in these patients [10]. HIV infection is associated with quantitative and qualitative gradual reduction of CD4 cells, so the patient is at risk of many simultaneous and opportunistic infections [11]. These diseases are one of the most important factors in reducing the quality of life and mortality in patients with HIV/AIDS [12]. Antiretroviral therapy, specifically followed and implemented since 1996, can reduce the incidence of opportunistic infections in these patients and increase their survival [13]; therefore, early diagnosis and minimizing the interval between the diagnosis of HIV infection and the emergence of clinical symptoms of AIDS can be of great importance. This study aimed to determine the survival rate and mean interval between the diagnosis of HIV infection and the emergence of clinical

symptoms of AIDS in patients who referred to Yazd Behavioral Hygiene Center from January 2003 to 2017 to provide information that would help health care system's planners and decision makers of the country.

In similar Iranian studies conducted by Moshrefi et al [14], Shahi et al. [15], and Baba-Mohammadi [16], the most commonly reported HIV transmission method was contaminated syringes. The same result was obtained in this study, and the most common transmission method of HIV infection included contaminated syringe (65%), sexual contact (28%), and mother-to-child transmission (5%) and other ways (1%), respectively.

In other countries, sexual transmission is the most commonly reported transmission method. For example, in Croatia, homosexual intercourse was reported as the predominant transmission method, but in Eastern Europe, injected drug abuse was reported as the main method [17]. In Africa, the most important transmission method was mother-to-child transmission [15].

As known, in our country, the main transmitting method of this infection is still the use of contaminated syringes in drug injection addicts, which involves a limited population of injectable addicts and can be cured by providing free syringes. But the next transmission method, unprotected sexual intercourse, threatens a larger population and has a higher risk.

Based on other findings in this study, the mean interval between diagnosis and observation of the first disease indicating AIDS was 2913 ± 232 days.

It was also found in the study of Babamahumudi et al. that the mean duration of diagnosis in patients with AIDS was 2.72 ± 1.45 years and for HIV-infected patients was 1.71 ± 0.48 years [16].

In the report of Pederson et al. (1989), the clinical symptoms of HIV patients emerged on average 670 days (45-1506 days) [18]. The results of the study by Chadborn et al. (2004) on 14158 patients to evaluate the delayed diagnosis of AIDS and its related mortality, showed that mortality rate of those with a delayed diagnosis was 10 folds in the first year than those diagnosed early with HIV [19]. Cheng et al. (2016) in a 5-year retrospective cohort study in China on 6737 patients, found that delayed diagnosis of the disease decreased [20]. Robertson et al. (2015) found that 48% of the patients accepted the disease and sought treatment late for personal reasons and suggested performing rapid diagnostic tests in high-risk groups as an effective measure to reduce the late-onset treatment in these patients [21]. Lin et al. (2017) reported in Thailand that receiving delayed treatment and care decreased in these patients, but many patients were still not diagnosed on time [22].

The results of this study showed a significant association in the mean interval between the time of diagnosis and the first diagnosis of AIDS between indigenous patients (3223 ± 247) and non-indigenous (1847 ± 448) cases. Indigenous patients were considered as patients who lived in Yazd province and most of non-indigenous patients referred to the centers of behavioral disease counseling in Yazd province from nearby provinces such as Sistan and Baluchestan and Kerman. One of the reasons for reducing the mean interval between the time of diagnosis and observing the first AIDS-related disease in this group of patients may be the lack of access to their expected services at their place of residence, which makes people face difficulties in receiving services, and travel a long distance and spend money, which delays receiving diagnostic and therapeutic services. People may also be reluctant to receive services in their own city, because of stigma caused by the disease.

Research by Merati et al. (2013) in Isfahan showed that the mortality of patients with AIDS was 36 years earlier than life expectancy in the general population [23]. Harrison et al. Also found that the years of potential life lost was about 11 years in patients with AIDS at the age of 60, and 8 years at the age of 70 [24]. In this study, survival of patients since diagnosis was 4338 ± 189 days.

To carefully study whether HIV transmission method affects the disease survival, we should remove the effect of other variables such as age, gender, etc., and then examine the role of this variable. In the present study, approximately 80% of the sexually transmitted infection was related to women and according to the results, the survival rate of women was less than that of men.

One of the major reasons for delayed treatment services was social stigma by the disease. Indeed, despite the fact that more than 30 years have passed since the first epidemic of this disease, there is still a major discrimination against patients with HIV, and the stigma associated with HIV is one of the conditions that has hindered the disease control [25]. AIDS is one of the diseases that affects the patients' mental and social health status, due to community misconceptions and causes many problems in the useful activities of patients [25] and makes them feel different from the norm [26]. As a result, it weakens the programs on prevention of disease spread, because people will be afraid of voluntary testing or obtaining information about the disease, thus they would hide their disease from others [27]. Sassani et al. (2013) also found that patients with AIDS will experience a wide range of problems after seeking information from others about their disease due to HIV-related stigma [25].

Another reason for the delayed health and medical care services is low awareness of patients and people at risk. Most studies conducted worldwide on perceived susceptibility of patients with AIDS address students. In some of these studies, students, despite high risk and unprotected sexual behavior, did not consider themselves susceptible to AIDS infection [28,

[29]. Fallahi et al. (2013) also found in a qualitative study on 32 men with HIV that despite high-risk sexual behaviors, they did not consider themselves susceptible to AIDS and had erroneous perception and belief for getting the disease [30].

CONCLUSION

According to what expressed, public education, screening by urgent tests on all individuals with an emphasis on high-risk individuals, increasing community's awareness to reduce the social stigma of the disease and extension of health care and behavioral disease counseling centers are strategies to reduce the interval between the time of infection and the emergence of disease symptoms. Currently, the New Health Services Package for Health Care Providers is intended to provide guidelines and protocols for screening and educating people in the community based on age groups, facilitating the access to immediate tests, and considering at least one behavioral counseling center in almost every city; most of the activities of counseling centers for behavioral diseases in Iran are based on the country's HIV/AIDS program guideline, including diagnostic laboratory services for referral of high-risk groups (passive diagnosis), counseling the high-risk groups to evaluate risk factors such as injecting drugs and prevention of virus transmission, counseling the newly identified cases for accepting the disease and transmission methods of the virus (including injecting drugs, use of a common syringe), prevention of pregnancy, and using condoms, conducting clinical examinations by the physician and preliminary tests, prevention or treatment of opportunistic infections, such as tuberculosis and pneumocystis gyrovirus, and ultimately starting antiretroviral therapy, if needed [31].

The results of this study and similar studies highlight the obvious principle that is necessary to minimize the interval between the viral infection and disease diagnosis to control the disease, improve the quality of life of patients, and reduce years of potential life lost and we should not delay follow up and treatment of the disease until one of the clinical signs of the disease develops. Considering the results of this study, it can be suggested that the screening level should be expanded with immediate tests in the community; the health and medical personnel should have sufficient knowledge about the disease, social stigma experienced by patients; and the main activities in these centers should be based on confidentiality and free services to encourage most people in the community to use these services. The study's limitations include cultural and social variables, especially the disease stigma, and the lack of cooperation of the patient in obtaining information about the first approach to patients suspected of HIV infection that could affect the outcomes of all AIDS-related studies, like ours.

ACKNOWLEDGEMENTS

REFERENCES

1. Hamada AJ, Esteves SC, Clinics AA, undefined. A comprehensive review of genetics and genetic testing in azoospermia. SciELO Brasil.
2. Ishikawa T. Surgical recovery of sperm in non-obstructive azoospermia. Asian journal of andrology. 2012;14(1):109.
3. Origin, migration, and proliferation of human primordial germ cells. 2013:19--37.
4. Jungwirth A, Giwercman A, Tournaye H, Diemer T, Kopa Z, Dohle G, et al. European Association of Urology guidelines on Male Infertility: the 2012 update. 2012;62(2):324-32.
5. Assche EV, Bonduelle Ma. Cytogenetics of infertile men. academicoupcom.
6. Bobadilla JL, Macek M, Fine JP, Farrell PM. Cystic fibrosis: A worldwide analysis ofCFTR mutations?correlation with incidence data and application to screening. Human Mutation. 2002;19(6):575--606.
7. Reproduction PNS, and Development F, undefined. Causes of azoospermia and their management. Csiro.
8. Carpi A, Sabanegh E, and Sterility JMF, undefined. Controversies in the management of nonobstructive azoospermia. Elsevier.
9. Reprod SCEA, undefined. Male infertility due to spermatogenic failure: current management and future perspectives. cbraorgbr.
10. Hecht NB. The making of a spermatozoon: a molecular perspective. Developmental genetics. 1995;16(2):95--103.
11. Baarends WM, der Laan R, Grootegoed JA. Specific aspects of the ubiquitin system in spermatogenesis. Journal of endocrinological investigation. 2000;23(9):597--604.
12. Sadowski M, Suryadinata R, Tan AR, Roesley SNA, Sarcevic B. Protein monoubiquitination and polyubiquitination generate structural diversity to control distinct biological processes. IUBMB Life. 2012;64(2):136--42.
13. Sun L, opinion in cell Biology ZJCC, undefined. The novel functions of ubiquitination in signaling. Elsevier.
14. Ramanathan HN, in b, molecular Biology YY, undefined. Cellular strategies for making monoubiquitin signals. Taylor \& Francis.
15. Sigismund S, Polo Sa. Signaling Through Monoubiquitination. 2004:149--85.
16. Eletr ZM, Wilkinson KD. Regulation of proteolysis by human deubiquitinating enzymes. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research. 2014;1843(1):114--28.
17. Wilkinson KD. Ubiquitination and deubiquitination: targeting of proteins for degradation by the proteasome. 2000;11(3):141--8.
18. Sato Y, Goto E, Shibata Y, Kubota Y, Yamagata A, Goto-Ito S, et al. Structures of CYLD USP with Met1-or Lys63-linked diubiquitin reveal mechanisms for dual specificity. Nature structural \& molecular biology. 2015;22(3):222.
19. Massoumi R. Ubiquitin chain cleavage: CYLD at work. Trends in biochemical sciences. 2010;35(7):392--9.
20. Carpi A, Sabanegh E, Mechanick JJF, sterility. Controversies in the management of nonobstructive azoospermia. 2009;91(4):963-70.
21. Stahl PJ, Masson P, Mielnik A, Marean MB, Schlegel PN, Paduch DAJF, et al. A decade of experience emphasizes that testing for Y microdeletions is essential in American men with azoospermia and severe oligozoospermia. 2010;94(5):1753-6.
22. Ranganathan P, Kattal N, Moustafa MH, Sharma RK, Thomas AJ, Agarwal AJF, et al. Correlation of nuclear factor kappa B (NFKB) with sperm quality and clinical diagnoses in infertile men. 2002;78:S95.
23. Pentikäinen V, Suomalainen L, Erkkilä K, Martelin E, Parvinen M, Pentikäinen MO, et al.
24. Wright A, Reiley WW, Chang M, Jin W, Lee AJ, Zhang M, et al. Regulation of early wave of germ cell apoptosis and spermatogenesis by deubiquitinating enzyme CYLD. Developmental cell. 2007;13(5):705--16.
25. Ni F, Zhao H, Cui H, Wu Z, Chen L, Hu Z, et al. MicroRNA-362-5p promotes tumor growth and metastasis by targeting CYLD in hepatocellular carcinoma. Cancer letters. 2015;356(2):809--18.
26. Li D, Jian W, Wei C, Song H, Gu Y, Luo Y, et al. Down-regulation of miR-181b promotes apoptosis by targeting CYLD in thyroid papillary

cancer. International journal of clinical and experimental pathology. 2014;7(11):7672.

27. Gao J, Huo L, Sun X, Liu M, Li Da. The tumor suppressor CYLD regulates microtubule dynamics and plays a role in cell migration. Asbmb.

28. Plant TM, Marshall GRJEr. The functional significance of FSH in spermatogenesis and the control of its secretion in male primates. 2001;22(6):764-86.

29. Zirkin BR, editor Spermatogenesis: its regulation by testosterone and FSH. Seminars in cell & developmental biology; 1998: Elsevier.

30. Eelaminejad Z, Favaedi R, Sodeifi N, Gilani MAS, Shahhoseini MJRbo. Deficient expression of JMJD1A histone demethylase in patients with round spermatid maturation arrest. 2017;34(1):82-9.

31. Medrano J, Marques-Mari A, Aguilar C, Riboldi M, Garrido N, Martinez-Romero A, et al. Comparative analysis of the germ cell markers c-KIT, SSEA-1 and VASA in testicular biopsies from secretory and obstructive azoospermias. 2010;16(11):811-7.