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Trend analysis of AIDS mortality and years of life lost from 2004 to 2019 in southern Iran

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Abstract

Introduction: This study aimed to determine the mortality rate and years of life lost (YLL) due to acquired immunodeficiency syndrome (AIDS) in southern Iran.

Material and methods: All deaths from AIDS in Fars province were obtained from electronic population-based death registration system (EDRS). Crude mortality rate, age-standardized mortality rate (ASMR), YLL, and YLL rate data were calculated. Joinpoint regression method was used to examine the trend.

Results: During the 16-year study period (2004-2019), 663 deaths caused by AIDS occurred in Fars province. Of these, 89.4% (593 cases) were men, and 57.3% (380 cases) were 30-44 years old. The total YLL due to AIDS during the study period was 13,232 in men and 1,569 in women. Based on joinpoint regression analysis, the rate of YLL due to premature mortality remained stable over 16 years. The annual percent change (APC) for males was 0.2%, with a 95% confidence interval (CI) of –6.4 to 7.1 and a *p*-value of 0.960. For females, the APC was 5.2%, with a 95% CI of –5.7 to 17.3 and a *p*-value of 0.337.

Conclusions: While there was a decrease in crude and standardized mortality rates and YLL related to AIDS in men, there was an increase in these rates among women. However, the changes in trends were not deemed statistically significant. Political commitment and effective technical strategies are needed to prevent the occurrence of this disease through continuous care services.

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Key words: AIDS, mortality rate, years of life lost, joinpoint regression, Iran.

Introduction

Human immunodeficiency virus (HIV) infection remains a significant contributor to worldwide mortality. As of the end of 2016, approximately 36.7 million individuals were living with HIV globally [1]. Additionally, that year saw 1.6 million new HIV infections and one million HIV-related deaths [2]. According to statistics from 2015, most people living with HIV (PLHIV) as well as new HIV infections and deaths related to HIV/acquired immune deficiency syndrome (AIDS) were located in sub-Saharan

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Africa [3]. Though there was a decrease in the occurrence of new HIV infections and related deaths between 2000 and 2017, the number of individuals living with HIV increased by 14% between 2010 and 2017, suggesting that the HIV/AIDS epidemic is still spreading [4]. The rise in the number of infections can be attributed to two factors, i.e., HIV leads to a long-lasting disease as it establishes a permanent reservoir in memory Th cells, and antiretroviral therapy (ART) is now widely accessible. Attention improves the longevity of PLWH [1]. The Joint United Nations Program on HIV/AIDS (UNAIDS) established the 90-90-90 targets in December 2013. The first "90" of the UNAIDS 90-90-90 goal is for 90% of all PLHIV to know their HIV status, the second "90" is for 90% of diagnosed PLHIV to be on ART, and the third "90" aims to achieve viral suppression among 90% of those on treatment [2].

The HIV epidemic significantly impacts human societies, both directly and indirectly. However, estimating the exact burden is challenging due to various complex factors. It has been observed that as the prevalence of HIV infection rises, there is a decrease in the gross domestic product (GDP). In the last decade, there has been a significant rise in global funding to combat HIV. The international expenses for HIV have been on the rise, with a 11% increase in 2011 compared with 2010, amounting to $16.8 billion. However, international aid remain almost stagnant, and a few donor countries have even reduced their budgets [3].

There was an estimated number of 39,000 AIDS-related deaths in the Middle East and North Asia that nearly doubled between 2001 and 2012, while worldwide, it declined by 16% [4]. The largest HIV epidemic in the Middle East is in Iran [5]. In the Islamic Republic of Iran, 61,000 people were infected with HIV in 2018, whereas recently, 4,400 people were added to this number and 2,600 people died from AIDS-related illnesses. Furthermore, the death rate due to AIDS has increased by 8% since 2010 [6].

HIV/AIDS-associated stigma is still one of Iran's leading public health concerns. From 2010 to 2019, epidemiological studies have shown that stigma and discrimination among Iranian individuals living with HIV/AIDS have caused several issues for patients. These problems include hindering their access to healthcare services, including antiviral treatment [7]. Assessing the society's health status and identifying its challenges can be performed by considering years of life lost (YLL). The World Health Organization's report states that one year of life is worth three times more than the GDP per capita of any country [8]. Therefore, this study was conducted to analyze the trend of mortality and years of life lost due to AIDS in Fars province, Iran.

Material and methods

From 2004 to 2019, a cross-sectional study was conducted in the Fars province that is located in southern Iran; it is the 4th largest province of Iran in terms of area and population [9] (suicide, n = 15). The studied population was 3,636,605 in 2004 and 4,147,239 in 2019. Data of all deaths related to AIDS were gathered from population-based electronic death registration system (EDRS). These data were sorted by age, sex, and year of death, and coded with number of ICD-10 (B20-B24). The EDRS system compiles information from various sources to record and collect data on deaths accurately. Deaths with similar fathers' names and national numbers were excluded from the study to avoid duplications.

The population of Fars province was calculated using data from health centers and census records from 1996 to 2016 while considering the annual population growth. The estimate was standardized according to the 2013 standard population for countries with low to moderate income [10].

Statistical analysis

During the study period, crude and age-standardized mortality rates (ASR) of AIDS were calculated based on sex and year of death. To calculate YLL, standard life table was used to determine life expectancy for various age and sex groups. Also, the number of AIDS-related deaths in each age and sex group was determined based on the following formula [11]:

$$YLL = N\,Ce^{(ra)} / (\beta + r)^2\,[e^{-(\beta + r)(L + a)}\,[-(\beta + r)(L + a) - 1] - e^{-(\beta + r)a}\,[-(\beta + r)\,a - 1]]$$

where N is number of deaths in a certain age and gender group, L is the standard life expectancy of deceased according to age group and gender, r is the discount rate of 0.03, β is the conventional rate in calculating age value that equals to 0.04, C is the age weight correction factor of 0.165, a is the age at death, and e is the Euler's constant nearly equal to 2.71828.

First, YLL was calculated according to 18 age groups: 0-4, 5-9, 10-14, etc., up to 85 years old, and then based on age groups of 0-4, 5-14, 15-29, 30-44, 45-59, 60-69, 70-79, and over 80 years, data were shown in a figure. Data analysis was done using a YLL template developed by the World Health Organization in an Excel spreadsheet, version 2016. A log-linear model was employed with joinpoint regression to analyze changes in crude and age-standardized mortality and YLL rates for various years. This method helps identify changes in trends over different periods and measure the degree of increase or decrease in each segment. An annual percent change described the trend line between join points (APC) based on the slope of the line segment and the average annual percent change (AAPC). The trend analysis was conducted using the joinpoint regression software 4.9.1.0.

Results

During the 16-year study period (2004-2019), 663 deaths caused by AIDS occurred in Fars province. Of these, 89.4% (593 cases) were men, and 57.3% (380 cases) were between

Table 1. Crude and age-standardized mortality rate (per 100,000 population) and years of life lost due to AIDS by sex and year in Fars province during 2004-2019

Year	Number of deaths		Crude mortality rate (per 100,000)		ASMR* (95% CI)		Years of life lost due to AIDS			
							No.		Per 1,000	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
2004	35	1	1.88	0.05	1.99 (1.37-2.61)	0.04 (0.01-0.07)	790	25	0.42	0.01
2005	11	2	0.59	0.11	0.54 (0.19-0.89)	0.14 (0.01-0.27)	268	41	0.14	0.02
2006	16	2	0.86	0.11	0.97 (0.55-1.40)	0.09 (0.02-0.16)	362	51	0.19	0.02
2007	30	6	1.60	0.32	1.55 (0.98-2.13)	0.29 (0.03-0.55)	696	135	0.37	0.07
2008	76	2	4.20	0.10	3.55 (2.64-4.45)	0.13 (0.01-0.25)	1,803	32	0.95	0.10
2009	66	6	3.46	0.31	3.15 (2.32-3.99)	0.27 (0.02-0.52)	1,527	150	0.80	0.07
2010	55	4	2.85	0.21	2.52 (1.76-3.27)	0.19 (0.01-0.37)	1,288	97	0.66	0.05
2011	26	0	1.33	0	1.14 (0.63-1.35)	0	605	0	0.31	0
2012	26	7	1.32	0.35	1.10 (0.59-1.61)	0.33 (0.06-0.59)	455	126	0.23	0.06
2013	36	4	1.80	0.20	1.54 (0.95-2.13)	0.14 (0.02-0.26)	792	80	0.39	0.04
2014	35	6	1.73	0.30	1.42 (0.85-1.99)	0.24 (0.01-0.47)	774	144	0.38	0.07
2015	19	1	0.92	0.04	0.76 (0.34-1.17)	0.04 (0.01-0.07)	419	24	0.20	0.01
2016	28	5	1.34	0.24	1.14 (0.64-1.64)	0.25 (0.04-0.46)	572	115	0.27	0.05
2017	50	1	2.40	0.04	2.00 (1.33-2.66)	0.03 (0.00-0.06)	1,097	25	0.52	0.01
2018	62	14	2.96	0.68	2.59 (1.85-3.33)	0.57 (0.21-0.93)	1,339	338	0.64	0.16
2019	22	9	1.04	0.44	0.98 (0.55-1.42)	0.39 (0.10-0.68)	445	186	0.21	0.09
Total	593	70	1.88	0.22	1.67 (1.52-1.82)	0.21 (0.15-0.27)	13,232	1,569	0.42	0.05
p-value	–	–	0.765	0.354	0.976	0.448	–	–	0.960	0.337

**Age-standardized mortality rate.*

30 and 44 years old. As can be seen in Table 1, the crude mortality rate due to AIDS in men was 1.88 in 2004 and 1.04 in 2019 per 100,000 population:, with AAPC = 0.9% (95% confidence interval [CI]: –5.4-7.7, $p = 0.765$). Whereas in women, it was 0.05 in 2004 and 0.44 in 2019 per 100,000 population, with AAPC = 6.0% (95% CI: –6.9-20.6, $p = 0.354$). The standardized mortality rate in men decreased from 1.99 in 2004 to 0.98 in 2019 per 100,000 population: AAPC = –0.2% (95% CI: –6.3-6.3, $p = 0.948$), while in women, it increased from 0.04 in 2004 to 0.39 in 2019 per 100,000 population: AAPC = 4.9% (95% CI: –7.8-19.4, $p = 0.437$) (Table 1).

The total years of life lost due to AIDS during the 16-year study period were 13,232 (0.42 per 1,000 people) in men, 1,569 (0.05 per 1,000 people) in women, and 14,801 (0.23 per 1,000 people) in both sexes, with male-to-female sex ratio of 8.4 (Table 1). The average number of years of life lost due to AIDS was 22.3 years for men and 22.4 years for women. The highest and lowest number of deaths in both

sexes were in the age groups of 30-44 years and 0-14 years, respectively (Figure 1).

Temporal trends of AIDS mortality by age groups

In the 0-44 age group, there were stable trends in men, with AAPC = –0.4% (95% CI: –7.6-7.3, p = 0.911) and in women, with AAPC = 12.9% (95% CI: –2.2-30.4, p = 0.091). In the 45-59 age group, there were stable trends in men: AAPC = 2.5% (95% CI: –5.5-11.1, p = 0.528) and in women: AAPC = 0.5% (95% CI: –21.7-28.9, p = 0.967). In the 60-74 age group, there were stable trends in men, with AAPC = 6.7% (95% CI: –21.2-44.4, p = 0.653) and in women, with AAPC = 17.7% (95% CI: –8.2-50.7, p = 0.181). In the +75 age group, there were stable trends in men: AAPC = 21.6% (95% CI: –13.4-70.8, p = 0.238) and in women: AAPC = –4.1% (95% CI: –27.1-26.1, p = 0.748).

The age group with the highest YLL rate for both sexes was the 30-44 years group, and the lowest YLL for men was the 70-79 years group, while for women, it was the over 80 years group (Figure 2).

Based on the joinpoint regression analysis, it was found that the YLL rate due to premature mortality remained stable over 16 years. The annual percent change (APC) was 0.2% (95% CI: –6.4-7.1, p = 0.960) for males, 5.2% (95% CI: –5.7-17.3, p = 0.337) for females, and 0.9% (95% CI: –5.1-7.4, p = 0.753) for both sexes. The model did not show any joinpoint, hence, the average annual percent change (AAPC) was the same as APC (Figures 3 and 4).

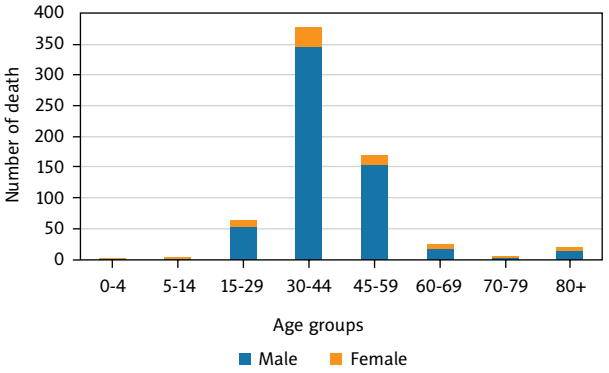


Figure 1. Number of AIDS-related deaths according to gender and age groups

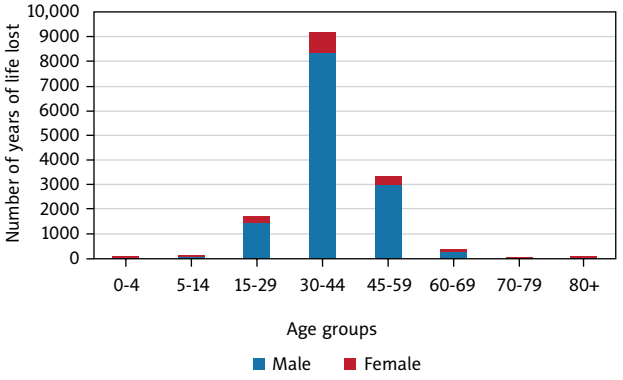
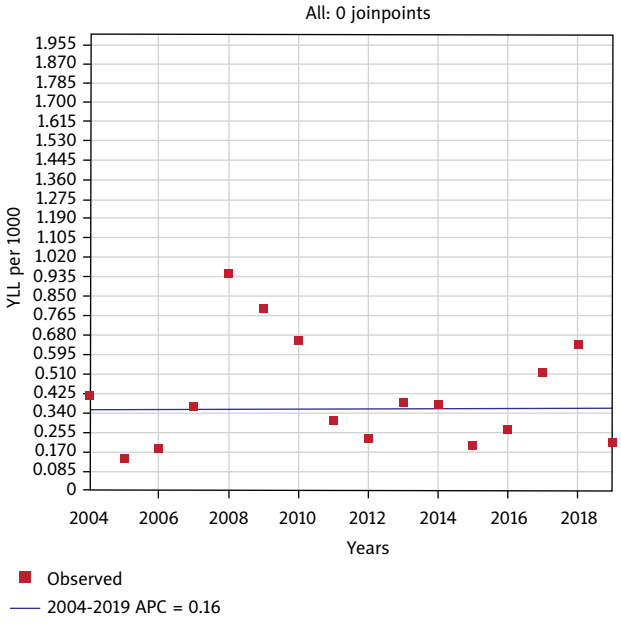
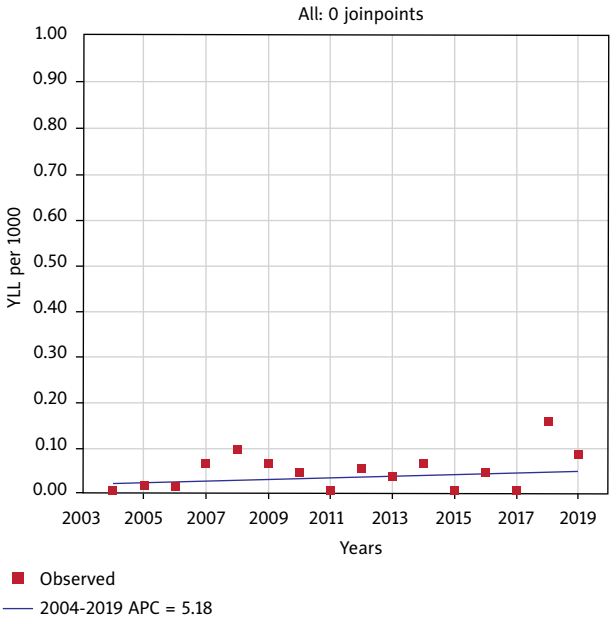


Figure 2. Years of life lost due to AIDS according to gender and age groups



**Indicates that the annual percent change (APC) is significantly different from 0 at the a = 0.05 level Final Selected Model: 0 Joinpoints.*

Figure 3. Trends in the number of years of life lost due to AIDS in men during the years 2004-2019



**Indicates that the annual percent change (APC) is significantly different from 0 at the a = 0.05 level Final Selected Model: 0 Joinpoints.*

Figure 4. Trends in the number of years of life lost due to AIDS in women during the years 2004-2019

Discussion

HIV and AIDS are a range of conditions caused by HIV infection [12].

This study was conducted to determine the trend of mortality rate and years of life lost due to AIDS from 2004 to 2019 in southern Iran. The results of our study revealed that during the study period, the mortality rate was higher in men than in women, and the highest number of deaths occurred in the age group of 30 to 44 years.

Other studies have confirmed this finding. A survey conducted in America reported that 81% of all HIV infections diagnosed in the United States among adults and adolescents occurred in men [13]. In Nigeria, a higher percentage of people with AIDS were men, and most sufferers were adults over years old [14]. The results of a study conducted in Latvia (northern Europe) also showed that both the number of deaths and the number of potential years of life lost were 3 times higher in men than in women [15], which was likely related to gay men. After sex workers, male-to-male sex is the second risk factor for AIDS [14]. The death rate due to HIV reflects the pattern of population groups that are most affected by the HIV/AIDS epidemic.

The results of our study revealed that the crude mortality rate due to AIDS in men decreased from 1.88 in 2004 (per 100,000 population) to 1.04 in 2019 (per 100,000 population), while in women, it was 0.05 in 2004 (per 100,000 population) and reached 0.44 in 2019 (per 100,000 population). The age-standardized mortality rate in men decreased from 1.99 in 2004 to 0.98 in 2019 per 100,000 population, whereas in women, it increased from 0.04 in 2004 to 0.39 in 2019 per 100,000 population.

This result is consistent with findings of other studies, showing that the mortality trend in HIV-infected patients has decreased in the last 20 years [16-18]. A study conducted in England and Wales observed that all-cause mortality among people with HIV infection aged 15-59 years decreased over the decade. The death rate from HIV decreased from 217 per 10,000 in 1999 to 82 per 10,000 in 2008. This decrease has been seen in all age groups except women aged 50-59 years [17]. One of the reasons for this may be related to early diagnosis and treatment of CD4+ cell count. Previous cohort studies have provided evidence of the impact of late diagnosis on all-cause mortality, demonstrating that CD4+ cell count at treatment initiation is the most important prognostic factor [19-21]. Moreover, the death rate in HIV patients diagnosed later was ten times higher than in those diagnosed on time [22]. Recent modeling work suggested that the death rate among people with HIV is approaching that of the general population. These predictions assumed that HIV-infected individuals are diagnosed early and have rapid access to antiretroviral treatments [23, 24]. The higher the availability of antiretroviral drugs, the closer the death rate due to HIV to the general population.

The results of our study showed that the years of life lost due to AIDS during the 16-year study period were 0.23 per 1,000 people in both sexes, with male-to-female sex ratio of 8.4. The average number of years of life lost due to AIDS was 22.3 years for men and 22.4 years for women.

Another study conducted in Iran reported that the total number of years of life lost in 2016 was approximately 0.36 per 1,000 people while in 2008, it was approximately 0.37 per 1,000 individuals, which decreased comparing with 2008 [25]. In sub-Saharan Africa, the YLL rate was 2.41, in South Asia it was 0.37, and in Latin America it was 0.36 per 1,000 people [26]. In 2017, the age-standardized YLL rate per 1,000 population due to HIV/AIDS was 6.5 worldwide [27]. Considering that sub-Saharan Africa is one of the most infected regions in the world regarding HIV infection, the difference in the number of years of life lost between Iran and this region is consistent. Also, there is considerable heterogeneity among countries in terms of years of life lost, with differences reflecting the measures taken to control AIDS as well as the behavioral characteristics of different countries.

Furthermore, the results of our study demonstrate that the years of life lost in men are eight times more than that in women. This finding can be justified due to the higher prevalence of HIV in men than in women. The results of previous studies show that the incidence and prevalence of the disease are higher in men than in women. A study conducted in England confirmed that male patients were infected with HIV more than twice compared with female patients [17]. In America, there were more male HIV patients than females infected with HIV, with a significant difference between the number of men and women contracting the disease [28]. Because there are more male patients than female ones, the mortality rate and the years of lost life are higher in men than in women.

Although this study is of high quality, with a strong study design, large sample size, and extensive time period of data analysis, a limitation is that the YLL rate was not evaluated throughout the whole of Iran due to the unavailability of necessary data.

Conclusions

Even though the trend of crude and age-standardized mortality rates and years of life lost due to AIDS decreased in men and increased in women, the differences were not statistically significant. Also, the crude mortality rate was constant in all age groups. Based on the results of the study, more attention should be paid to the increasing trend of HIV infection in women, and to improve efforts to control the disease, especially among women. Therefore, political commitment and effective technical strategies are needed to prevent HIV/AIDS, providing timely, effective, and continuous care services and tools, such as syringes, needles, and condoms for high-risk groups, including sexually active women. Future analytical studies are recommended to provide more insights on this field.

Disclosures

1. Institutional review board statement: This study was approved by the Ethics Committee of Shiraz University

of Medical Sciences, with approval number IR.SUMS.REC.1399.772.
2. Assistance with the article: We would like to acknowledge the Health Vice-Chancellor, Shiraz University of Medical Sciences.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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