Original Article
http://mjiri.iums.ac.ir
Medical Journal of the Islamic Republic of Iran (MJIRI)

Med J Islam Repub Iran. 2021(1 Dec);35.159. https://doi.org/10.47176/mjiri.35.159

Trend Analysis of HIV/AIDS Burden in Iran: Results from the Global Burden of Disease 2017 Study

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Received: 7 May 2021 Published: 1 Dec 2021

Abstract

Background: Despite global efforts, human immunodeficiency virus/ acquired immunodeficiency syndrome (HIV/AIDS) is still one of the major public health problems in the entire world. In this context, assessing the burden of this disease in different parts of the world is of great importance. In this study, we aimed to investigate the trends of HIV/AIDS incidence and mortality in Iran during 1990 and 2017.

Methods: The HIV/AIDS burden data, including the age-standardized incidence rate (ASIR) and the mortality rate (ASMR), was extracted from the Global Burden of Diseases 2017 study for the total Iranian population and by gender from 1990 to 2017. The trend analysis was performed using joinpoint regression modeling approach.

Results: The obtained results showed that in 2017, the HIV/AIDS ASIR and ASMR were, respectively, more than 12 and 10 times of these rates in 1990. Also, the estimated average annual percent change (AAPC) was 9.8% and 8.7%, respectively for the ASIR and the ASMR. In this period, women have experienced a sharper slope of ASIR and ASMR trends compared with Iranian men.

Conclusion: The increasing trend of HIV/AIDS burden is a serious alarm for the Iranian health policymakers. To achieve the United Nations Programme on HIV and AIDS goals, there is an urgent need for an efficient national action plan that breaks the HIV/AIDS taboo in the society, promote access to HIV testing and prevention facilities, especially among the key populations, and provide care and treatments for all infected people.

Keywords: HIV/AIDS, Incidence, Mortality, Trend Analysis, Iran

Conflicts of Interest: *None declared*
Funding: *None*

Cite this article as: Balooch Hasankhani M, Zayeri F, Rasouli M, Salehi M. Trend Analysis of HIV/AIDS Burden in Iran: Results from the Global Burden of Disease 2017 Study. *Med J Islam Repub Iran.* 2021 (1 Dec);35:159. https://doi.org/10.47176/mjiri.35.159

Introduction

Acquired immunodeficiency syndrome (AIDS) is known as one of the most important health challenges in different parts of the world (1). Although a short time has passed since the first case of human immunodeficiency virus (HIV) infection, the world has been faced with an epidemic for which there is no definitive or specific cure yet (2). AIDS is not limited to a certain geographical region or race, and all social groups, especially the youth, are vulnerable to it (3). The overall rate of people living with HIV is rising worldwide because of extending the antiretroviral therapy (ART) coverage, challenging human communities with its health-related, socioeconomic, cul-

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↑What is "already known" in this topic:
The trend of AIDS burden has been already investigated in some parts of the world, including our country, Iran. The previous researches about the burden of HIV/AIDS in Iran have generally used descriptive statistical approaches and showed an increasing pattern during the last decades.

→What this article adds:
In the present study, we used more advanced inferential statistical methods to model the trend of HIV/AIDS burden in Iran over a 28-year period. The applied statistical technique allows us to determine the existing change points and estimate the slope of trend in different time intervals.

tural, and political consequences (1, 4).

Since the outset of this epidemic, 75.7 million people have become infected with HIV, and 32.7 million people have died as a result of AIDS-related diseases. In 2019, there were 38 million people living with HIV/AIDS all over the world, including 1.8 million children <14 years. Despite these worrisome statistics about the HIV/AIDS in different parts of the world, there is some good news about reducing the burden of this disease in recent decade. New cases of HIV were 2.8, 2.1, and 1.7 million in 1998, 2010, and 2019, respectively (a reduction of 40% over the 2 last decades and about 20% reduction over the last decade). In addition, about 700,000 AIDS-related deaths were recorded globally in 2019 compared with 1.1 million deaths in 2010 (about 36% reduction) (5).

Depending on the study population, study period, and the main outcome under study, the published research in the field of HIV/AIDS burden in Iran have reported different patterns in the trend of incidence, prevalence, mortality, and disability-adjusted life year rates. For instance, a study by Noori et al showed that the burden of HIV/AIDS has dramatically increased from 1990. This disease was known as the 152nd leading cause of disease burden in 1990, while it was ranked as the 37th cause in 2010 (6). In another study by Moradi et al, they reported a nonsignificant increase in HIV/AIDS incidence and mortality rates in the period 2008-2016 (7). A trend analysis between 1990 and 2015 by Moazen et al revealed that the HIV/AIDS mortality had a peak in 1995 followed by a steady decline until 2015 (8). A number of studies are also available in the different Iranian key populations, which show a downward trend in the HIV/AIDS burden over the last decade (9-11).

Joinpoint models are used in many fields of statistical research, such as generalized linear models, risk function models, time series, nonparametric methods, and longitudinal studies. The joinpoint regression has had many applications in medical, biological, animal, plant, and genetic sciences, and the problem of estimating the number of joinpoints in the joinpoint regression model by Kim in 2000 has been stated. In 2000, Kim used a series of permutation tests to determine the number of unknown change points in connection with the joinpoint regression (12). The National Cancer Institute still uses this method among all available methods to track cancer mortality, prevalence, and survival in the United States. Regarding these controversial findings, we decided to use the global burden of disease (GBD) data set as one of the most comprehensive and reliable sources in the field of disease burden and apply more advanced statistical approaches to model the trend of HIV/AIDS incidence and mortality rates during 1990 and 2017 in Iran.

Methods

Data Sources

In this research, we extracted the HIV/AIDS incidence and mortality rates from the GBD 2017 study (13). The GBD estimates and reports the burden of disease indices, including incidence, prevalence, mortality, years of life lost, years lived with disability, and disability-adjusted life years, for a wide range of diseases and injuries by gender and age group for 195 world countries between 1990 and 2017. The GBD data base is an open access source that is freely available for any research-related activities. In the present study, we used the aggregated age-standardized HIV/AIDS incidence and mortality rates per 100,000 Iranian people for the total population and by gender from the GBD database during 1990 and 2017. As no personal data were used in this research, informed consent was neither required nor necessary.

Statistical Analysis

The joinpoint regression modeling is a well-known statistical technique for the analysis of trend data. In this statistical approach, a log-linear Poisson regression is utilized in which the change points are identified using the Mote Carlo permutation test. To capture the jump locations (change points) in the trend data, a segmented linear regression model is fitted (14). More formally, suppose a set of observations $(x_1, y_1), (x_2, y_2), \dots, (x_n, y_n)$, where x_i represents the study time points and y_i indicates the HIV/AIDS incidence or mortality rates. The joinpoint regression model is defined as:

$$y_i = \beta_0 + \beta_1 x_i + \gamma_1 (x_i - \tau_1)^+ + \cdots + \gamma_k (x_i - \tau_K)^+ + \varepsilon_i, \qquad i = 1, \dots, n$$

where $\tau_k, k = 1,2, \dots, K$ represents the location of change point, K shows the number of change points, and ε_i indicates the error term of the model. In addition, $\beta_0, \beta_1,$ and $\gamma_1, \dots, \gamma_k$ indicate the regression coefficients. Here, the notation $(x_i - \tau_k)^+ = x_i - \tau_k$ if $x_i - \tau_k > 0$, and $(x_i - \tau_k)^+ = 0$ otherwise. In the present study, the regression coefficients and the number of change points were estimated using the mythology introduced by Kim et al (12). To interpret the estimates, some useful indices, such as the annual percent change (APC) and the average annual percent change (AAPC) can be reported. Clearly, the APC shows the annual percent change of the HIV/AIDS incidence or mortality rates and the AAPC is a summary measure of the trend over a fixed interval (1990-2017). This index enables us to interpret the average APCs over a period of time using a single measure. The joinpoint regression modeling was performed using the Join point Regression Program Version 4.8.0.1 (Statistical Research and Applications Branch, National Cancer Institute) (15). P<0.05 was considered statistically significant.

Results

Table 1 shows the trend of HIV/AIDS age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) in Iranian population by gender for some specific years. In addition, Figure 1 displays these trends for the time period under the study, separately for men, women, and the total population. One can observe that the HIV/AIDS ASIR has increased from 0.29 in 1990 to 3.58 per 100,000 in 2017. This means that the HIV/AIDS ASIR in 2017 was more than 12 times of this rate in the starting point of the study. Moreover, the HIV/AIDS ASIR in 2017 was 7.6 and 28.5 times of this rate in year 1990, respectively, for men and women. Over this period of time, the HIV/AIDS ASMR has increased from 0.09 in 1990 to

[DOI: 10.47176/mjiri.35.159]

Table 1. Trend of HIV/AIDS ASIR and ASMR in Iranian population by gender

Index	Gender	Year						
		1990	1995	2000	2005	2010	2015	2017
ASIR	Male	0.45	0.65	1.58	1.45	2.09	2.96	3.43
	Female	0.13	0.20	0.56	0.72	1.38	2.85	3.71
	Both	0.29	0.42	1.08	1.09	1.74	2.91	3.58
ASMR	Male	0.14	0.23	0.39	0.68	0.80	0.96	1.01
	Female	0.04	0.07	0.13	0.26	0.36	0.62	0.77
	Both	0.09	0.15	0.26	0.47	0.58	0.79	0.90

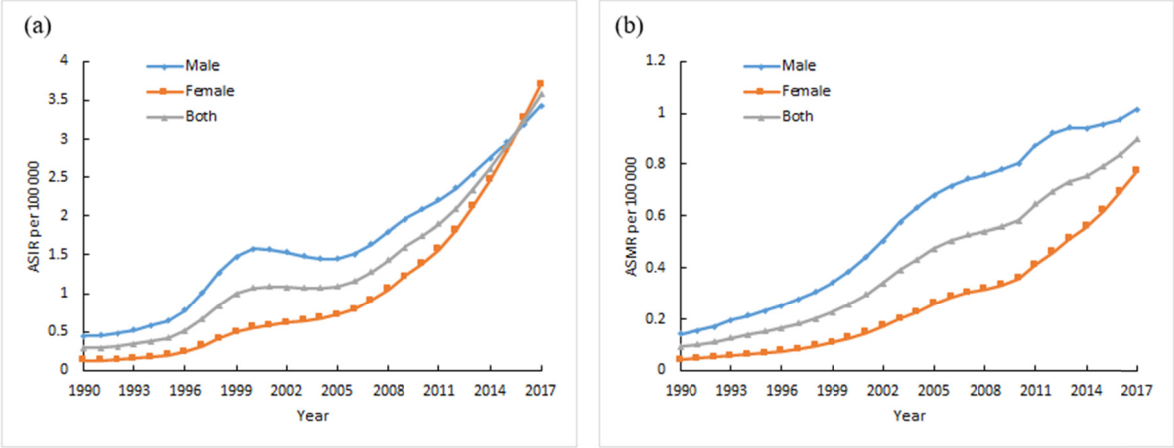

Fig. 1. HIV/AIDS ASIR and ASMR trend in Iranian population from 1990 to 2017 (a: ASIR, b: ASMR)

0.90 per 100,000 in 2017. Also, it was found that the HIV/AIDS ASMR has increased from 0.14 in 1990 to 1.01 in 2017 for men and from 0.04 in 1990 to 0.77 per 100,000 in 2017 in women. This means that the HIV/AIDS ASMR in 2017 was about 7.2, 19.2, and 10 times of this rate in 1990, respectively in men, women, and the total Iranian population.

In the next step of the data analysis, to capture the observed turning points in ASIR and ASMR trends (Fig. 2), we fitted different joinpoint regression models to the data, separately for men, women, and the total population. The modeling process has led to different turning points and APCs for these trends. Table 2 and Figure 2 show the results of fitting 6 joinpoints regression models to the HIV/AIDS ASIR and ASMR trends data. The fitted model to the total population ASIR data has resulted in 4 significant joinpoints in 1992, 1995, 1999, and 2006, which leads to 5 periods with different trends. In this context, the obtained results could be interpreted in terms of the estimated APCs and AAPC. The estimated APCs show annual percent change of 3.7, 10.7, 25.3, 1.4, and 10.9 in HIV/AIDS ASIR, respectively, in the time intervals of 1990-1992, 1992-1995, 1995-1999, 1999-2006, and 2006-2017. Moreover, the estimated AAPC implies a mean annual rise of 9.8% in HIV/AIDS ASIR for the total Iranian population. The interpretation of the estimates based on the fitted models for men and women is quite similar. Here, comparing the estimates for men and women indicates that Iranian women had higher APC values than men in all the determined time intervals with the F/M AAPC ratio of 1.7.

Based on the fitted model to the total population ASMR data, 2 significant joinpoints were identified in 1998 and 2004, which leads to 3 periods with different trends. The estimated APCs show an annual percent change of 10.1, 14, and 5.5 in HIV/AIDS ASMR, respectively, in the time intervals of 1990-1998, 1998-2004, and 2004-2017. The estimated AAPC suggests a mean annual rise of 8.7% in HIV/AIDS ASMR for the total Iranian population. The F/M AAPC ratio of 1.5 was also estimated based on the fitted models.

Discussion

In recent years, higher accessibility to HIV preventive and diagnostic services, more efficient treatments and medications and promoting the level of patients' care made HIV/AIDS more manageable and increased the survival rate of the patients dramatically. However, it still remains as one of the major health problems throughout the world. According to the World Health Organization (WHO), the HIV/AIDS key populations can be defined as men who have sex with men, people who inject drugs, prisoners, and people in other closed settings, sex workers and their clients, and transgender people (16). These key populations play an important role in the current status of HIV/AIDS burden in our country, Iran. In general, our findings in the present study revealed an ascending trend for the incidence and mortality of this disease in Iran over the past 3 decades. Some of the important reasons for these upward trends in Iranian population are as follow:

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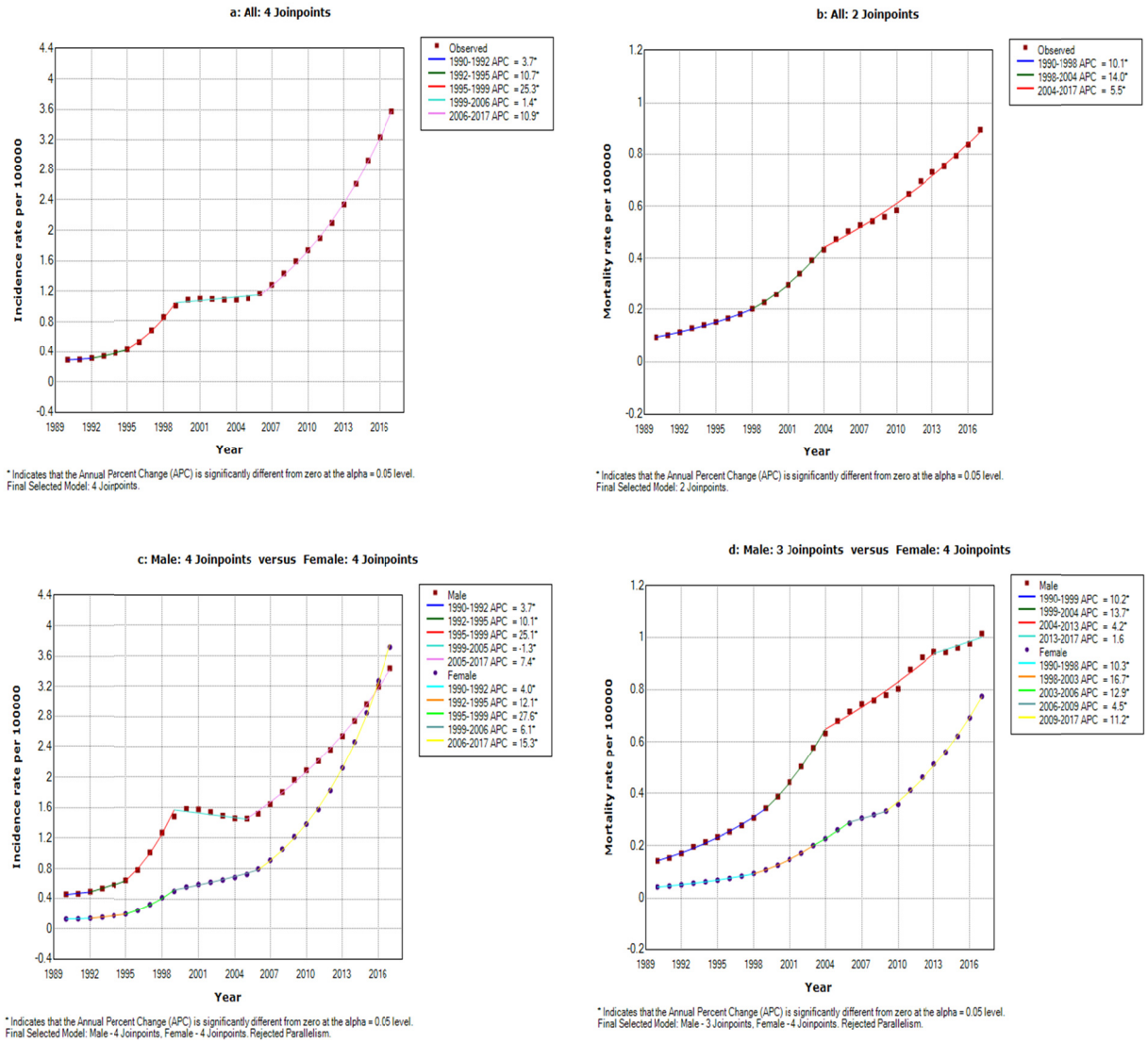

Fig. 2. Model-based estimates of HIV/AIDS ASIR and ASMR over 1990-2017 (a: total population ASIR, b: total population ASMR, c: ASIR by gender, d: ASMR by gender)

Table 2. Joinpoint regression estimates for HIV/AIDS ASIR and ASMR data in Iranian population from 1990 to 2017

Segments	Total population		Males		Females	
	Year	APC (95 % CL)	Year	APC (95 % CL)	Year	APC (95 % CL)
ASIR						
Trend 1	1990-1992	3.7* (0.5, 7.1)	1990-1992	3.7* (0.2, 7.3)	1990-1992	4.0* (1.1, 7.0)
Trend 2	1992-1995	10.7* (7.3, 14.3)	1992-1995	10.1* (6.4, 13.9)	1992-1995	12.1* (9.0, 15.4)
Trend 3	1995-1999	25.3* (23.3, 27.3)	1995-1999	25.1* (23.0, 27.2)	1995-1999	27.6* (25.8, 29.4)
Trend 4	1999-2006	1.4* (0.9, 1.9)	1999-2005	-1.3* (-2.1, -0.6)	1999-2006	6.1* (5.6, 6.6)
Trend 5	2006-2017	10.9* (10.7, 11.2)	2005-2017	7.4* (7.2, 7.6)	2006-2017	15.3* (15.1, 15.5)
AAPC	1990-2017	9.8* (9.3, 10.3)	1990-2017	7.8* (7.3, 8.4)	1990-2017	13.3* (12.9, 13.8)
ASMR						
Trend 1	1990-1998	10.1* (9.4, 10.8)	1990-1999	10.2* (9.6, 10.7)	1990-1998	10.3*(9.9, 10.8)
Trend 2	1998-2004	14.0* (12.5, 15.4)	1999-2004	13.7* (11.9, 15.6)	1998-2003	16.7* (15.4, 18.0)
Trend 3	2004-2017	5.5* (5.2, 5.8)	2004-2013	4.2* (3.6, 4.8)	2003-2006	12.9* (9.0, 17.0)
Trend 4	-	-	2013-2017	1.6 (-0.0, 3.3)	2006-2009	4.5* (0.9, 8.3)
Trend 5	-	-	-	-	2009-2017	11.2* (10.8, 11.6)
AAPC	1990-2017	8.7* (8.3, 9.1)	1990-2017	7.5* (7.0, 7.9)	1990-2017	11.4* (10.7, 12.0)

* Significant at alpha=0.05

First, drug trafficking was a major problem for the Iranian governments in the previous decades because of its geographical location and about 2000 km border with the most important opium producer country in the world, Afghanistan, which produces more than 80% of the global heroin. Also, Iran has a long common border with Pakistan as one of the major transit countries for illegal drugs in the world. According to some reports, more than 75%

[DOI: 10.47176/mjiri.35.159]

of the produced narcotic drugs in Afghanistan is smuggled through Iran and Pakistan (17). The increasing rate of narcotic addiction, especially through sharing the injection instruments, is the result of the high purity and availability of heroin with a low price in Iran, which has led to an increase in the number of drug user prisoners. As a result, the injection of narcotics is the most common route of HIV/AIDS transmission in Iran. However, a considerable reduction in the number of Iranian infected individuals was reported by 2 different studies among people who inject drugs in the recent years. They suggested that this reduction is a consequence of developing extensive harm reduction programs in Iran (9, 11).

Second, AIDS is a taboo in Iran because of religious beliefs and cultural norms, and people with HIV/AIDS are faced with stigma and prejudice. Therefore, people usually hide their disease from others, which subsequently leads to an increase in the risk of HIV/AIDS transmission. Hiding diseases because of social stigma will also result in the lack of public access to counseling and diagnostic services in high-risk groups. Thus, late detection of HIV will lead to the progression of the disease to AIDS, and increasing the risk of transmission and early mortality (8, 18).

Third, regarding the defined key populations by the WHO, men who have sex with men, sex workers and their clients as well as transgender people are 3 subpopulations who constantly stigmatized by other people, especially by conservative and religious parts of the population. In addition, prostitution and homosexuality are illegal in Iran, and some homosexual activities might be sentenced to death penalty. Consequently, people's fear of disclosure and social stigma motivates them to hide these kinds of activities. As a result, a considerable number of HIV/AIDS patients in these key populations do not receive preventive, therapeutic, and supportive services, and this increases the risk of infection in population.

Finally, some other reasons may contribute to increasing the trend of HIV/AIDS incidence in Iranian population. Progress in diagnostic techniques, shortage of educational and preventive programs, having unprotected sexual intercourse with the spouse or with others, lack of knowledge, attitude and practice among people who infected with HIV, and people's unawareness of their infection with HIV/AIDS (less than 40% Iranian patients are unaware of their infection) are some of these reasons (19, 20).

Comparing the changes in the annual incidence of HIV/AIDS tells us that the highest annual percentage change was related to the third period (1995-1999) with APC = 25.3 and the fourth period (1999-2006) had the lowest change with APC = 1.4. The marked increase in the incidence rate in the third period may be due to the second wave of epidemic, which started from 1991 among addicted people to narcotic injection with high-risk behaviors like sharing infected syringes and needles. In this period of time, more than 80% of the HIV cases were addicted to drug injection, and unfortunately this situation was extended to the prisons (11, 21). In the last decade of the previous century, most of activities in HIV monitoring system have been focused on identification of high-risk places, such as prisons and places of narcotic use, and reporting the detected HIV/AIDS cases in these areas.

In addition, the lowest rate of increase in HIV/AIDS incidence in the fourth period was probably due to the national strategic plan for HIV infection control. In this period of time, the triangular clinics (to prevent AIDS, drug addiction, and sexually transmitted diseases) were started in Kermanshah province and expanded to other parts of the country. After establishment of voluntary counseling and testing (VCT) centers in most provinces and cities, the distribution of disposable syringes and needles in prisons and the promotion of educational programs led to more success in reducing infection in injecting drug users and prevented the vast transmission of HIV in the society (22). As a result of administration of these programs, the percentage of HIV/AIDS cases among injecting drug users was reduced from more than 80% in 1991 to about 60% in 2013 (21).

Following the considerable reduction in the annual rate of HIV/AIDS incidence over the fourth period, the annual incidence rate had a sharp raise, with an APC of 10.9 over the fifth period (2006-2017). This upward trend may be attributed to the third wave of epidemics resulting from unprotected sexual intercourse. The use of amphetamine-type stimulants might be considered as one of the main reasons for increasing the rate of unprotected sexual behaviors, especially among the younger individuals in this period of time (22).

In the present study, we found that the HIV/AIDS incidence rate in Iranian women was remarkably lower than in men, while Iranian women had higher annual percent changes over the study period (the estimated F/M AAPC ratio of 1.7). These findings are in agreement with the obtained results from a study in 2014 that reported a noticeable increase in the trend of identifying new cases among women. According to their reports, the percentage of infection in the newly identified female cases has increased from 4% in 2001 to 22% in 2011 (21, 7). Women are at risk of HIV/AIDS, especially in marital relations. Some studies in Iran have shown that three fourth of women with HIV/AIDS have been infected by their spouses (23). Gender inequality and gender-based violence, absence of comprehensive sexual and reproductive health services, illiteracy, and lack of knowledge and practice about preventive behaviors are some of possible reasons for the increased women's vulnerability to HIV/AIDS (24). In addition, poverty drives some women to prostitution, which increases the risk of HIV/AIDS infection. The growing number of HIV/AIDS cases among women will also increase the risk of mother-child contagion, as another important transmission route of this disease.

The results of the present study indicated that the mean HIV/AIDS mortality rate has annually increased over the study period by 8.7% for the total population, 7.5% for men, and 11.4% for women. Apparently, the rising number of mortality cases might be attributed to people's lack of awareness of their HIV/AIDS infection and hiding the disease because of social stigma, as well as the inadequate coverage of antiretroviral therapy (18, 19).

Regarding the mean annual changes in HIV/AIDS mor-

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tality rates, it was found that the highest and lowest changes were related to the second (1998-2004) and third (2004-2017) periods, respectively with APC = 14 and APC = 5.5. The small increase in HIV/AIDS mortality rate in the last 14 years of the study could be due to improving the awareness about HIV/AIDS among patients and the entire society, promoting the level of patients' care as well as wider use of ART in Iran.

Similar to the findings for the HIV/AIDS incidence, our results showed that the HIV/AIDS mortality in female patients was lower than in male patients during 1990 and 2017. However, female patients have experienced a sharper slope of annual increase in death from HIV/AIDS compared with male patients (AAPC of 11.4 in women versus AAPC of 7.5 in men).

According to our calculations on GBD 2017 data, the HIV/AIDS mortality in the Middle East and North Africa (MENA) region has a rising trend, with an AAPC of 7%. With an AAPC of 8.7%, Iran stands above the average annual percent change of HIV/AIDS mortality estimated for the MENA countries. According to the Joint United Nations Programme on HIV and AIDS (UNAIDS) reports in 2019, the global HIV/AIDS incidence has declined by 23% compared with 2010 and 40% reduction has been observed compared with the peak in 1998. In addition, deaths from HIV/AIDS have decreased by 39% and 60%, respectively, from the peak in 2004 and 2010 compared with 2019. Although this decline seems to be a hopeful global message, it is not adequate to achieve the 90-90-90 goals for 2020 (5).

Here, it should be noted that the lack of access to local comprehensive and reliable data about burden of HIV/AIDS in Iran is the most important limitation of our work. In addition, the HIV/AIDS burden data sets are highly confidential in our country and the independent researchers have limited access to them. Thus, we used the estimated data by the GBD 2017 study as an international open access source to achieve our goals. Despite this limitation, our work is the first research in analyzing the HIV/AIDS burden over the span of almost 3 decades in Iran. Using an advanced statistical technique (joinpoint regression model) for analyzing the GBD data could be thought as another strength of the present study.

Conclusion

In general, our findings indicated that the HIV/AIDS incidence and mortality had a growing trend during 1990 and 2017 in Iran. These findings seem to be worrisome, since the global trend of HIV/AIDS burden had a downward trend from 2010. Poverty, stigma and other social and cultural inequalities play important roles in upward trend of HIV/AIDS in our country. To achieve the 90-90-90 goal of UNAIDS, the Iranian health policymakers should put more efforts on promoting the knowledge of patients and the entire society about this disease and improving the access to prevention and control facilities, especially in the key populations as well as providing the proper care and treatment for the infected individuals.

Acknowledgments

The authors would like to express their gratitude to the Staff of the School of Public Health, Iran University of Medical Sciences, for their assistance in conducting this study.

Availability of Data and Materials

The HIV/AIDS burden data are freely accessible in the GBD compare website (available at http://ghdx.healthdata.org/gbd-results-tool). Requests for additional information should be addressed to the corresponding author.

Ethics Approval and Consent to Participate

This research was conducted based on the data from GBD 2017 study, which is an open access online data source. The ethical aspects of the present study were approved by the Ethics Committee of the Iran University of Medical Sciences (project code: 99-1-2-18396, Ethics code: IR.IUMS.REC 1399.979).

Conflict of Interests

The authors declare that they have no competing interests.

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[DOI: 10.47176/mjiri.35.159]