

Original Article

An Alarming Shift of HIV Infection from Injection Drug to Sexual Transmission in Mashhad, Iran, 1989-2014

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ABSTRACT

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Introduction: Iran is facing to a rapid change in the epidemiological pattern of HIV. The trend of annual number of new HIV infections and factors associated with the development of HIV over the last two decades in Iran, were examined.

Methods: The data were retrospectively collected from patients who attended the Behavior Diseases Consultation Center of Mashhad University of Medical Sciences in Iran. Individuals were contributed if they were HIV-positive. Baseline factors including demographic, behavioral and clinical characteristics for all participants were examined. Changes in population characteristics were assessed using chi-square test or the Fisher's exact test.

Results: From 1989 to 2014, 584 individuals were eligible for present analysis according to the inclusion criteria. Most patients were men (87%) with most being 36–52 years old, unemployed (58%), married (39.3%), less educated (47.7%) and had a history of imprisonment (83%). The most common modes of HIV transmission were injection drug use (IDU) (51.4%) and IDU along with the sexual relationship (26.5%). These transmission modes varied significantly according to gender (p -value<0.001). Similarly, IDU and sexual relationship were most important transmission modes in males and females, respectively. The number of new HIV infections through sexual-related modes has risen sharply in recent years.

Conclusion: In Iran, the pattern of HIV transmission is shifting from unsafe injection drug to unsafe sexual contact for forthcoming years. Also, increasing trend of HIV incidence in women is remarkable. Accordingly, HIV-prevention strategies need to be changed.

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Introduction

The HIV pandemic is steadily increasing worldwide in the last four decade. Although the annual number of AIDS-related deaths are decreasing in many countries, the danger for the Middle East and North Africa (MENA) is serious.¹

The Joint United Nations Program on HIV/AIDS (UNAIDS) estimated that 38 million (31.6-44.5 million) people were living with HIV at the end of 2019. Of these people, 240000 (170000–400000) were living in MENA. In recent years, global efforts to strengthen HIV prevention and treatment programs are reducing the rate of HIV transmission, AIDS-related deaths, and new HIV infections. Meanwhile, new infections in 2019 increased by 22% compared to 2010, but, AIDS-related death only 2% decrease in MENA.²

According to WHO estimation, number of people living with HIV in Iran (a country in the Middle East) until 2019 was 59000(33000-130000).³ In Iran the HIV burden is concentrated among people who inject drugs (PWID) and is quite low in the general population.⁴⁻⁷ However, the number of people living with HIV and new HIV infections have been growing. In 2005, the prevalence in the general population for the age ranged 15-49, was 0.1% while it is expected to rise to 0.16% by 2020.⁸ The first case of HIV/AIDS in Iran was observed in a six-year-old child with hemophilia through contaminated blood products in 1986. These imported blood products caused large numbers of hemophiliacs to become infected with HIV. It was the first wave of the epidemic of the country.^{9,10} The second wave of this disease occurred with the outbreak of the epidemic of 1996 in some of Iran's penitentiaries among

PWID because of insecure use of intravenous drugs. The number of new HIV infections suddenly increased considerably and this trend continued and reached a peak by 2004.^{6,8} Although the prevalence of HIV among PWID has been declining, it remains one of the most important factors fueling the epidemic in Iran.⁴ Alongside with decrement, the third wave of the epidemic can be attributed to sexual transmission of HIV. The number of recorded cases through sexual relationship is gradually increasing.¹¹ Evidence shows that the increase in the number of new cases of pregnant women living with HIV has increased the birth rate of children with this disease.^{8,10} This phenomenon may be called the beginning of the fourth wave of HIV outbreaks.

Generally, the HIV transmission routes among all registered cases from 1986 to 2014 were shared equipment in injecting drug users (67.2%), sexual relationships (13.9%), blood products (0.9%), mother-to-child (1.3%) and unknown (16.7%).⁸ Nowadays the rate of HIV transmission through sexual relations is rising. It is a big warning that the transmission trend is shifting from injecting drug users to sexual relationships.^{12,13} It is also worth noting that alongside an increase in the sexual transmission rate, the number of infected women is also rising in recent years. More than 35% of newly diagnosed cases are women.^{8,14}

Given the importance of the incremental growth of HIV and a limited number of studies in the northeast of Iran; the present paper examines trend, new infections, epidemiological findings and factors associated with HIV prevalence in these patients between 1989 and 2014 in the northeast of Iran, Razavi Khorasan Province.

Materials and Methods

Ethics Statement

The study was approved by the ethical committee of Mashhad University of Medical sciences in Iran (IR.MUMS.REG.1392.807).

Study design and participants

This study was a retrospective study among HIV-positive cases diagnosed during the period 1989-2014 and referred to the Behavioral Diseases Consultation Center (BDCC) of Mashhad University of Medical Sciences in the Razavi Khorasan province, Iran. Participants included in the study consisted of 1) volunteers who attend after a high-risk behavior; 2) referrals of new HIV cases come from various organizations such as Mashhad prisons, blood transfusion organization, hospitals, and clinics and so on.

HIV Testing

HIV testing can be conducted for surveillance, diagnosis or blood screening purposes.¹⁵ In the case of voluntary individuals, a blood specimen was collected after pretest counseling and was later tested for free HIV testing. Initially, a rapid test was performed as a screening. Then, if the result of the rapid test was positive, ELISA and Western Blot testing was done as the confirmatory test in accordance with the national HIV testing algorithm.¹⁶ These people receive post-test counseling by on-site counselors and are monitored for HIV care at the center. All tests were performed at the center's Laboratory so that the results could quickly be returned to the participants. Patient's information was strictly confidential. In the

case of referrals, the diagnostic documents of the HIV testing were taken from individuals.

All subjects completed a structured questionnaire programmed into the interviewers in face-to-face interview. The registry also tracks patient vital status, including date of death, the cause of death (when available), and place of death. Individuals return almost every 1 month to assess their physical health, mental, medical treatment and some laboratory testing (eg. CD4 counts).

Study eligibility

Subjects were excluded if the results of the confirmatory HIV testing were negative for them. Also, non-Iranian people from the study were excluded.

Statistical analysis

Demographic characteristics (age, date of birth, sex, marital status, employment status, educational status and prison record) and clinical characteristics (HIV diagnosis date, routes of HIV transmission, and ART treatment history) have been collected for each subject. We categorized the age HIV diagnosis into groups (≤ 14 years, 15–24 years, 25–49 years and ≥ 50 years).

At first, data were entered and cleaned. For continuous variables, median and interquartile range (or mean and standard deviation) were calculated. Categorical factors associated with HIV infection were summarized using frequency and percentage stratified by the gender. Then, were tested using the chi-square test or the Fisher's exact test. Time trend for HIV transmission by gender and risk factor using linear charts was examined. Non-missing data in the included/relevant variable(s) were

investigated. All analyses were conducted with SPSS software, version 20 for Windows. A two-tailed p-value of less than 0.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics

Among the 606 individuals recorded in the study, 22 were excluded from the present analysis for the following reasons: Eighteen patients were non-Iranian in nationally and four individuals were diagnosed HIV-negative in later confirmatory testing. The final analysis population consisted of 584 individuals that met the eligibility criteria.

The median age of patients was 44 years (IQR: 36-52). The most of patients were male (87%), and for them, median age was 45 years (IQR: 37-52). In terms of job status, 58% of the participants self-identified as unemployed. Housewives and students were also considered unemployed. More than half of these patients (54.1%) had completed only primary-level education and 39.7% were currently married. Eighty-three percent of the patients had a history of imprisonment. For 22.6% of patients, treatment was started. At the end of the study, 173 patients were alive (29.6%) and 176 patients (30.1%) dead. There was no information available on the status of other patients. This lack of information is due to the fact that 30.8% of patients came from other Iranian provinces to the center and returned to their city after treatment or diagnosis. A number of patients were also homeless people who did not have a stable place to live.

The median age of the HIV diagnosis was 35 years (IQR: 28-40). The HIV prevalence was highest in the age group of 25-49 years, which

is 83.6% of the study population.

Baseline CD4 cell counts (1st available count after HIV diagnosis) were available for 277 individuals (47%); the median CD4 cell count was 382 cells/mm³ (IQR: 213.5-585). The demographic and clinical characteristics were not statistically significant by the gender except for educational status and CD4 level (Table1).

Relationship between Mode of HIV transition and Gender

Table 2 presents the modes of HIV transition. The most important transmission modes were IDU (51.4%) and unsafe sexual contact along with IDU (26.5%). The history of imprisonment was high among PWID (91.7%) but lower in those infected through sexual relationships (28.6%). There was a statistically significant association between the gender and mode of HIV transition ($P < 0.001$). In other words, the most frequent mode of HIV transition in male and female was IDU and through a spouse, respectively.

Time Trends in new HIV infections by gender and modes of transmission

Table 3 describes the number of new HIV infections by the modes of HIV transition between 1989 and 2014. It was observed that in the early years (1989-1993), the infected blood product was the most important factor in the spread of the disease. Also, transmission of disease from these people to their spouse has led to the further spread of the disease.

In 1996, HIV transmission risk among IDUs suddenly increased and reached 22 cases (95.7%) of the total number of cases in that year. Following the trend of the disease, since 2003, the rate of incidence steadily has grown

Table 1. Demographic and Clinical Characteristics of HIV/AIDS patients by sex, Mashhad, 1989-2014

	Male n (%)	Female n (%)	Total n (%)	P value ^a
Marital status				<0.001
Married	185(39.3)	28(43.1)	213(39.7)	
Single	161(34.2)	7(10.8)	168(31.3)	
Divorced	120(25.5)	17(26.2)	137(25.6)	
Widow	5(1.1)	13(20.0)	18 (3.4)	
Job status				<0.001
Unemployed	153(52.9)	46(82.1)	199(57.7)	
Employed	136(47.1)	10(17.9)	146(42.3)	
Educational status				0.192
Illiterate or Elementary	215(55.6)	21(42.9)	236(54.1)	
Intermediate	91(23.5)	15(30.6)	106(24.3)	
High school or Diploma	69(17.8)	12(24.5)	81(18.6)	
Higher than diploma	12(3.1)	1(2.0)	13 (3.0)	
History of imprisonment				<0.001
Yes	430(91.3)	12(19.4)	442(82.9)	
No	41(8.7)	50(80.6)	91(17.1)	
ART				<0.001
Yes	103(20.3)	28(38.9)	131(22.6)	
No	405(79.7)	44(61.1)	449(77.4)	
Age of HIV diagnosis				0.001
≤14	5(1.1)	3(4.5)	8(1.5)	
15-24	40(8.5)	12(17.9)	52(9.7)	
25-49	398(84.7)	51(76.1)	449(83.6)	
≥50	27(5.7)	1(1.5)	28(5.2)	
CD4 Level				0.394
≤200	54(23.8)	12(24.0)	66(23.8)	
201-349	51(22.5)	10(20.0)	61(22.0)	
350-500	57(25.1)	7(14.0)	64(23.1)	
≥501	65(28.6)	21(42.0)	86(31.0)	

^aP value from Chi-square test

Table 2. Distribution of transmission routs of HIV by sex, Mashhad, 1989-2014

Transmission routs of HIV	Male N=510 n (%)	Female N=74 n (%)	Total N=584 n (%)	P value ^b
IDU ^a	291(57.1)	9(12.2)	300(51.4)	
Unsafe sexual contac & IDU	13(2.5)	8(10.8)	21(3.6)	
Unsafe sexual contact	151(29.6)	4(5.4)	155(26.5)	
Blood products	9(1.8)	0(0)	9(1.5)	
Mother to child	3(0.6)	5(6.8)	8(1.4)	<0.001
through a spouse	3(0.6)	36(48.6)	39(6.7)	
Unknown	13(2.5)	5(6.8)	18(3.1)	
Other	27(5.3)	7(9.5)	34(5.8)	

^aInjection drug use

^bFisher's exact test for (r × c) table

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Table 3. Distribution of new HIV infections by year of diagnosis, Mashhad, 1989-2014

Transmission modes	Year											
	1989	1990	1991	1992	1993	1996	1997	1998	1999	2000	2001	2002
Total	3	2	1	5	2	23	27	96	16	8	13	15
Injection drug use	0(0)	0(0)	0(0)	1(20)	0(0)	22(95.7)	22(81.5)	91(94.8)	12(75)	3(37.5)	7(53.8)	8(53.3)
Unsafe sexual contact	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	2(2.1)	0(0)	0(0)	0(0)	3(20)
Injection drug use & Unsafe sexual contact	0(0)	0(0)	0(0)	0(0)	0(0)	1(4.3)	5(18.5)	1(1)	0(0)	0(0)	2(15.4)	4(26.7)
Blood products	3(100)	1(50)	1(100)	3(60)	1(50)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
Mother to child	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(6.3)	0(0)	0(0)	0(0)
Through a spouse	0(0)	1(50)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	3(18.7)	0(0)	0(0)	0(0)
Unknown	0(0)	0(0)	0(0)	1(20)	1(50)	0(0)	0(0)	1(1)	0(0)	5(62.5)	4(30.8)	0(0)
Other	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(1)	0(0)	0(0)	0(0)	0(0)

Table 3. (continued) Distribution of new HIV infections by year of diagnosis, Mashhad, 1989-2014

Transmission modes	Year											
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Total	19	21	33	41	38	37	24	31	24	46	41	a
Injection drug use	12 (63.1)	11 (52.4)	16 (48.4)	22 (53.7)	14 (36.8)	11 (29.8)	1 (4.2)	10 (32.3)	8 (33.3)	15 (32.6)	8 (19.5)	0(0)
Unsafe sexual cont	0(0)	1(4.8)	1(3)	1(2.4)	0(0)	2(5.4)	2(8.3)	1(3.2)	1(4.2)	2(4.4)	5(12.1)	0(0)
Injection drug use & Unsafe sexual contact	4 (21.1)	5 (23.8)	10 (30.3)	15 (36.6)	21 (55.3)	17 (45.9)	15 (62.5)	10 (32.3)	8 (33.3)	14 (30.4)	17 (41.5)	3 (7.5)
Blood products	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
Mother to child	0(0)	0(0)	0(0)	0(0)	0(0)	1(2.7)	0(0)	1(3.2)	1(4.2)	0(0)	2(4.9)	1(25)
Through a spouse	0(0)	2(9.8)	2(6.1)	2(4.9)	2(5.3)	4(10.8)	3(12.5)	4(12.9)	4(16.6)	7(15.2)	4(9.8)	0(0)
Unknown	3(15.8)	1(4.8)	2(6.1)	1(2.4)	0(0)	1(2.7)	2(8.3)	3(9.7)	1(4.2)	4(8.7)	2(4.9)	0(0)
Other	0(0)	1(4.8)	2(6.1)	0(0)	1(2.6)	1(2.7)	1(4.2)	2(6.4)	1(4.2)	4(8.7)	3(7.3)	0(0)

a, The end of the study was August 21, 2014. So, the statistics for 2014 was not complete.

through the unsafe sexual relationship that most of them occurred along with IDU. The proportion of sex-related factors increased from 21.1% to 53.7% in 2013, whereas the proportion of IDUs decreased from 63.2% to 19.5%. Also, as a new factor, several cases mother-to-child transmission has been seen

in recent years (2008, 2010, 2013 and 2014). As shown in Fig.1, the newly identified HIV infections of the disease between 1988 and 2014 varies by the IDU, sexual relationship and blood products. In the case of contaminated blood products, except for the early years, in the following years, the trend has been close to zero

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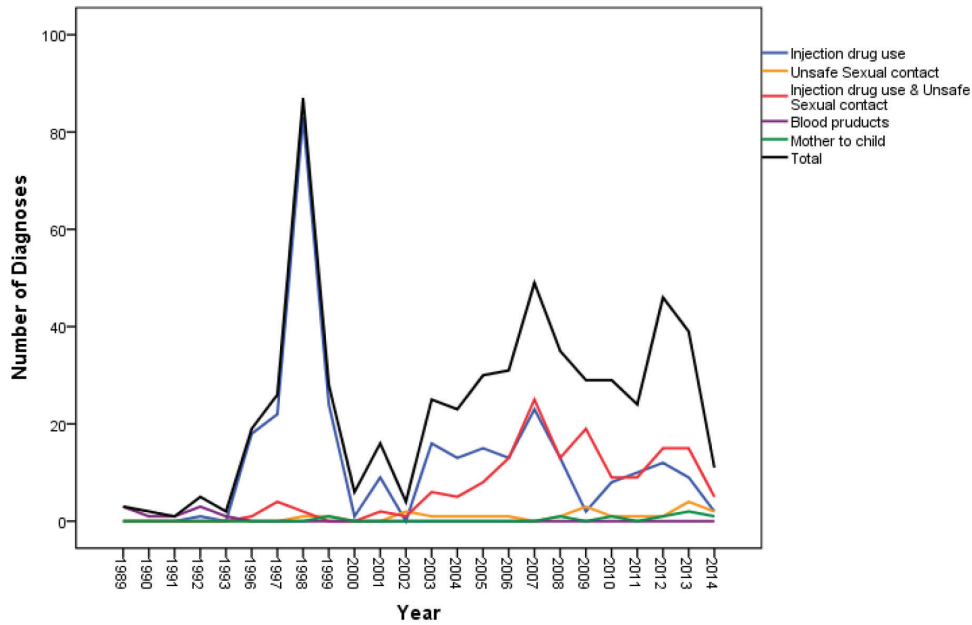


Figure 1. Trend of change in transmission routes of HIV from 1989 to 2014

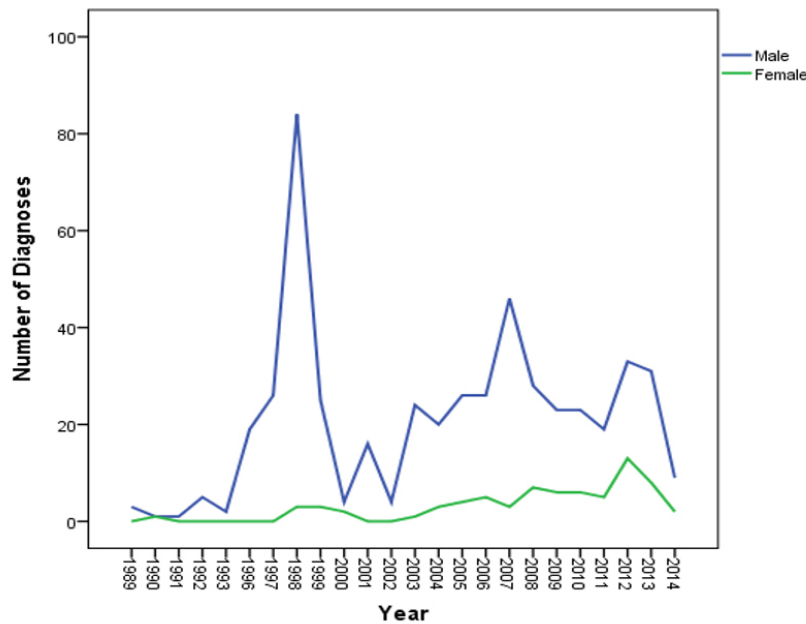


Figure 2. Trends of registered cases from 1989 to 2014 disaggregated by sex

and completely inhibited. HIV transmission through IDU hit a peak in 1998, possibly due to the HIV epidemic among PWIDs, especially in prisons in that year. Notably, since 2007, the trajectory of transmission due to IDU along with sexual relationship had a higher rate of

injecting drug alone. Attention to the gender-specific trends shows that proportion of men with this disease is still higher than women over time. However, the upward trend in the number of HIV-infected women in recent years is quite evident (Fig.2). Unfortunately, the records of

patients diagnosed in 1994 and 1995 were lost and not included in the analysis.

Discussion

Iran has previously been considered protected from HIV due to strong moral views. However, more recent evidence shows that Iran is facing to a rapid change in the epidemiological pattern of HIV. Although the most important mode of HIV transmission has been injection drug use over the years, sexually transmitted spread of HIV seems to be catching up.

According to the results of current study, most of patients were male, which is in line with national and global statistics.^{2,12,17} The reason for this may be to having the higher level of sexual immorality, multiple sexual partners, travel to foreign countries, and more drug use in men. However, it must be noted that this phenomenon may be due to less attending women to centers, especially since it is very difficult and sometimes impossible to reach high-risk groups such as female sex workers to counsel and encourage them to undertake HIV testing.

We found that most of the HIV-positive patients were infected in 25-49 age range. Compared with a recent study, the median age of HIV diagnosis in males was significantly higher than females (35 vs. 29 yrs).¹⁸ A review of the studies conducted in this area shows that in most cases, HIV disease has been acquired during youth years.^{19,20} The youths as an active age group and in the age of marriage and work are more likely to experience risky behaviors; hence, preventing these behaviors may reduce the prevalence of HIV remarkably in this group. Furthermore, the conflict with this disease affects the country's employment system and family life of these people. As a result,

management of high-risk behaviors related to HIV in young people is one of the priorities of public health.²¹

As evidence show, more than half of the patients were unemployed. Of course, it's important to note that even patients who have been registered as being employed are mostly seasonal and part-time workers, have not had much job stability, or have been nominated by their former job position. Previous studies have indicated that the incidence of this disease can affect the financial and occupational status of individuals and create instability.^{22,23} On the other hand, poverty and wealth inequality is a significant factor to explain the risk of developing HIV in the community.²⁴ Therefore, considering the employment status on the community level can be important in preventing the disease.

Overall, level of education in this study is low in line with other studies.^{18,25} It can be the indicator of low awareness of these people about their disease. Research shows that educated patients had a better quality of life because of the better job and financial conditions; higher levels of culture and better adaptation to disease.²⁵

In our findings, HIV is most commonly transmitted among PWIDs. Most of the research done so far has reported the results consistent with this result.^{5,26-31} Because of the neighborhood of Afghanistan and the fact that an important transit route for smuggling opiates pass through Iran, this country has the highest numbers of PWIDs among all countries in the MENA.^{6,30} Also, after the prevalence of HIV in 1996 among PWIDs in prisons, the rate of disease increased considerably. The HIV prevalence in these people has reached to 13.8% in 2014.⁸

On the other hand, sexual transmission of HIV in Iran has been steadily growing in recent years (32). Many studies have ranked sexual

transmission as the second transition mode of HIV.^{10,18,20,27} Evidence shows that, the use of amphetamine-type stimulants is rising that may be associated with high-risk sexual behaviors.^{33,34}

Also, the prevalence of HIV among FSWs has reached 4.5% and was more than three times among FSWs who had a history of IDU (comparable to HIV prevalence among PWID in Iran).³² As a result, it is reasonable to assume that great proportion of HIV infections among FSWs were acquired through IDU rather than unprotected sex. Thereafter, potentially, the risk of disease transmission of these people to their clients is high.

Our study indicated that in 26.9% of cases, patients have experienced high-risk sexual behavior in addition to IDU. We found that IDU was the most common transmission cause in males and sexual contact was the most common in females. So, a significant relationship was found between gender and transmission mode. These findings are similar to other reported results.^{10,20,35}

Based on results of this study, although the infection rate in men is higher than women, the proportion of female cases is increasing alongside the increase in the proportion of those infected by sexual route in recent years. This is compatible with previous studies.^{4,11,36} We found that most women are married and major transmission mode of HIV in them has been through their husbands, who were mostly PWID (48.6%) in consist with Nasirian et al.³⁷ Moreover prevalence of HIV among FSWs has led to an increase in the number of affected women.¹¹

As the number of women living with HIV grows, so does mother-to-child transmission, in the absence of adequate preventive measures. Although the rates of HIV transmission from

mothers to infants have decreased worldwide, MENA has had the least amount of progress in this field. In this region, nearly one-third of women living with HIV pass the virus on to their children.⁷ Our data show that rate of mother-to-child transmission is 1.4%. Similar researches certify this finding.^{20,31} Screening pregnant women for HIV lead to early detection of HIV infection and can reduce the risk of mother to child transmission.³⁸ In addition, use of antiretroviral medicines during the pregnancy and breastfeeding among women living with HIV prevents onward transmission of HIV.⁷ This is vital regard to the high-risk groups such as PWIDs and FSWs.

We found that 1.5% of our participants got the disease through blood products. It seems that activities to control HIV transmission through contaminated blood or blood products have been appropriate and approximately the number of cases of this way has dropped to zero.⁸

Based on our results and mentioned discussion above, it is apparent that the transmission pattern of HIV/AIDS is changing in Iran. Although previously IDU accounted for the major transmission route, this proportion will reduce in coming years and the third wave of infection through sexual contact may possibly be replaced by it.

During these years many policies have been implemented in relation to HIV. At first, the separation of HIV-infected prisoners with others caused to the stigma and discrimination of HIV-infected people. Later, Iran started harm reduction programs among high-risk groups (IDUs, prisoners, and more recently, FSWs) in 2001.³⁹ These programs include: needle, syringe, and condoms distribution program, provision of the condom to prevent unusual sex relationships, Methadone Maintenance Treatment (MMT) for IDUs and Voluntary

counseling and Testing Centers (VCT). FSWs, men who have sex with other men (MSMs) and their clients may play the role of a bridge across populations in transferring an HIV epidemic from high-risk groups to the general population. This fact should be considered by the main health policymakers in the country. Due to the lack of valid information regarding this group, and as they are one of the most hidden populations, epidemic of HIV in this group is uncertain but implementing serious harm reduction programs for them is important. In Iran, due to strong moral views, HIV was assumed to be less prevalent. Therefore, negative attitudes about ascertaining of disease to particular groups, guilty sufferers, being in the lower social level of infected people (IDUs, FSWs), pre/extramarital sex, homosexuality and like these led to HIV-related stigma. Stigmatized attitudes are serious obstacles to testing HIV, prevention, treatment, and support. It creates a hidden population that is extremely difficult to reach may restrict access to HIV-related data in conducting HIV researches in the region.³⁹⁻⁴¹

Conclusion

It is recommended that, in the case of Iran, HIV prevention and treatment strategies should be integrated within the existing religious, cultural and social context. Ignorance of the disease can lead to an HIV epidemic, which can affect people not associated with illicit sexual relations or drug use.

Limitations

There are some limitations to present study. First, it should be noted that HIV-positive people referring to other centers in other

provinces were not included in this study due to lack of availability. Then the results may not be generalized to all Iranian HIV/AIDS patients. Second, because of the stigma attributed to this disease and nature of interviewer-administered surveys, sensitive questions about personal sexual behaviors prevalence may underestimate the true values of these sexual behaviors.

In addition, since a large proportion of those present in the study have referred voluntarily, selection bias should also be considered as a possible limitation in the study.

Despite these limitations, this retrospective study was the first of its kind in Iran that investigated trends in HIV prevalence since the disease emergence so far on a provincial level. Moreover, the sample size of our study is relatively large.

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